EVALUATION OF CARDIOVASCULAR RISK IN OBESE INDIVIDUALS BASED ON LIPID PROFILE AND AUTONOMIC FUNCTION

Dissertation submitted to

THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY

In partial fulfillment of the
Regulations for the award of the degree of

M.D. (PHYSIOLOGY)
BRANCH - V

GOVT. CHENGALPATTU MEDICAL COLLEGE
THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY
CHENNAI, INDIA.

MARCH 2016

CERTIFICATE

This is to certify that this dissertation entitled **"EVALUATION OF CARDIOVASCULAR RISK IN OBESE INDIVIDUALS BASED ON LIPID PROFILE AND AUTONOMIC FUNCTION"** by the candidate **Dr.M.Ranjini Devi** for M.D (Physiology) Branch – V is a bonafide record of the research work done by her, under the guidance of **Dr.C.Hemachandrika M D., Associate Professor,** Formerly Head of the Department of Physiology, Chengalpattu Medical College, during the period of study (2013 - 2016), in the Department of Physiology, Chengalpattu Medical College, Chengalpattu. I also certify that this dissertation is the result of the independent work on the part of the candidate

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Chengalpattu.

DECLARATION

I hereby declare that this dissertation entitled **"EVALUATION OF CARDIOVASCULAR RISK IN OBESE INDIVIDUALS BASED ON LIPID PROFILE AND AUTONOMIC FUNCTION"** is a bonafide and genuine research work done by me under the guidance of our **Dr.C.Hemachandrika, M D.,** Associate Professor and Formerly Head of Department, Department of Physiology, Chengalpattu Medical College, Chengalpattu.

This dissertation is submitted to the Tamilnadu Dr. M.G.R Medical University, Chennai in partial fulfillment of the university requirements for the award of degree M.D in physiology.

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ACKNOWLEDGEMENT

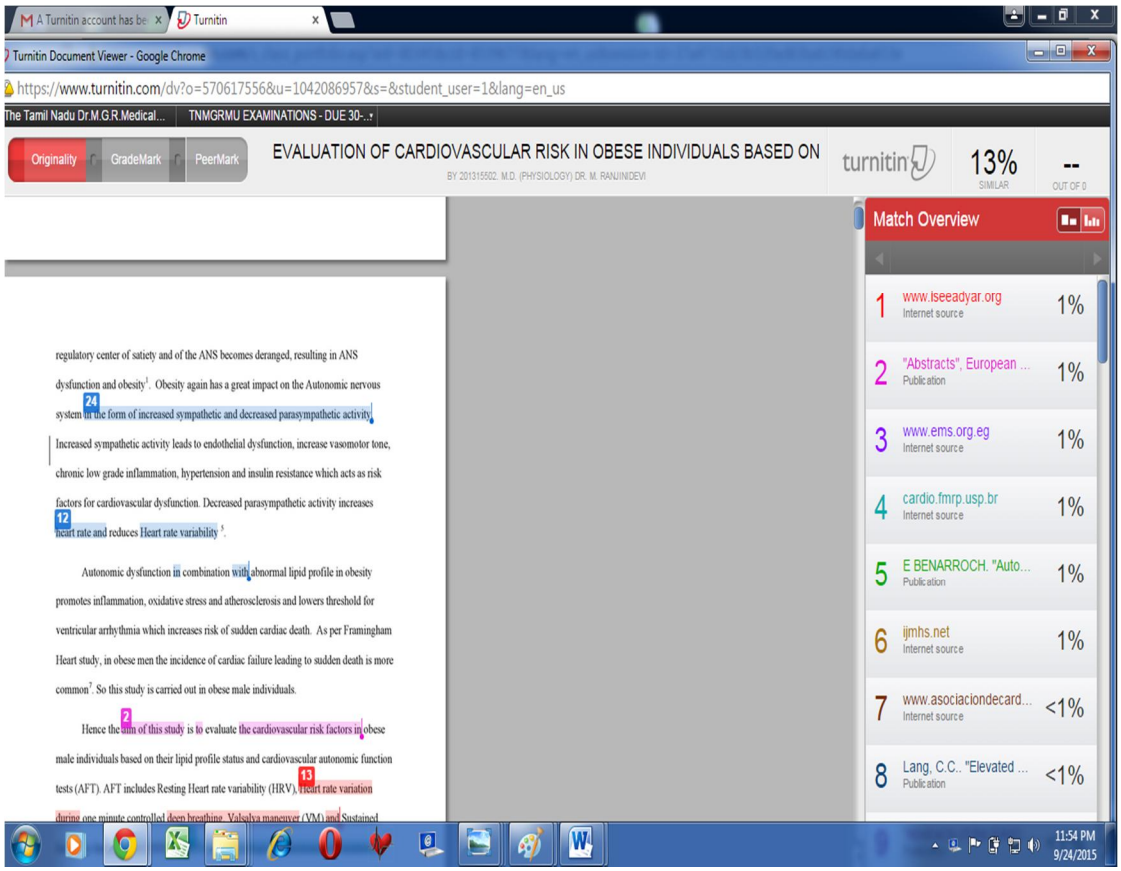
I express my profound gratitude to **Dr.K.Muthuraj, M.S**., the Dean of Govt. Chengalpattu Medical College and Hospital, Chengalpattu for permitting me to use all the needed resources for this dissertation work.

I sincerely express my grateful thanks to my **Prof. Dr.K.Muralikrishnan, M.D,** Head of Department of Physiology, Chengalpattu Medical College who has been a fatherly figure and without whom it would have been totally impossible to work on this subject. I thank him for being a constant source of encouragement, inspiration, not only in this study but in all my professional endeavors.

It is with deep sense of gratitude I acknowledge my profound indebtedness to **Prof. Dr. R. Kulothungan, M.D.,** Department of Medicine for providing cases for my study.

I express my sincere thanks to my Associate Professor, all the Asst. Professors, and Staff members, Dept. of Physiology, Chengalpattu Medical College, Chengalpattu.

I whole heartedly thank my subjects without whom this study would have been impossible.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regulatory center of satiety and of the ANS becomes deranged, resulting in ANS dysfunction and obesity[1]. Obesity again has a great impact on the Autonomic nervous system in the form of increased sympathetic and decreased parasympathetic activity. Increased sympathetic activity leads to endothelial dysfunction, increase vasomotor tone, chronic low grade inflammation, hypertension and insulin resistance which acts as risk factors for cardiovascular dysfunction. Decreased parasympathetic activity increases heart rate and reduces Heart rate variability [5].
Autonomic dysfunction in combination with abnormal lipid profile in obesity promotes inflammation, oxidative stress and atherosclerosis and lowers threshold for ventricular arrhythmia which increases risk of sudden cardiac death. As per Framingham Heart study, in obese men the incidence of cardiac failure leading to sudden death is more common[7]. So this study is carried out in obese male individuals.
Hence the aim of this study is to evaluate the cardiovascular risk factors in obese male individuals based on their lipid profile status and cardiovascular autonomic function tests (AFT). AFT includes Resting Heart rate variability (HRV), Heart rate variation during one minute controlled deep breathing, Valsalva maneuver (VM) and Sustained
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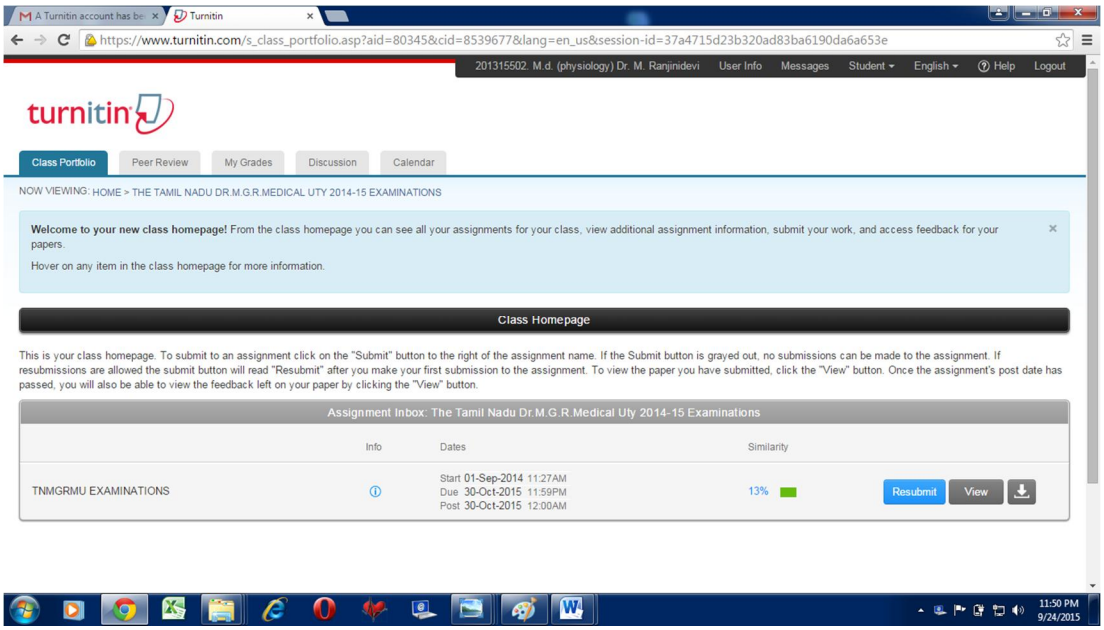
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MD Physiology
(2nd Year),
Chengalpattu Medical College,
Chengalpattu

Dear Dr.

The Institutional Ethical Committee of Chengalpattu Medical College reviewed and discussed your application to conduct the clinical / dissertation work entitled

"EVALUATION OF CARDIOVASCULAR RISK IN OBESE INDIVIDUALS BASED ON LIPID PROFILE AND AUTONOMIC FUNCTION".

ON 11.06.2014

The following documents reviewed

1. Trial protocol, dated _____version no
2. Patient information sheet and informed consent form in English and / or
   vernacular language.
3. Investigators Brochure, dated _____version
4. Principal Investigators current CV
5. Investigators undertaking

The following members of the Ethics committee were present at the meeting held on

Date 11.06.2014 Time 11.30 Noon Place Chengalpattu Medical College

Approved _____ Chairman Ethics Committee

_____ Member secretary of Ethics Committee.

Name of each member with designation:-

Clinical Members

1. Dr.R.Muthuselvan MD.,
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2. Dr.C.Srinivasan MD.,
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4. Dr.P.Parasakthi MD
   Prof & HOD of Forensic Medicine,CHMC

5. Member from Nongovernmental
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6. Philosopher : Mr.K.S.Ramprasad

7. Lawyer : Lr. I. M. Karimala Basha

8. Layperson : Mr.Dilli

We approve the clinical trial to be conducted in its presented form

The Institutional Ethics Committee expects to be informed about the progress of the study and any SAE occurring in the course of the study, any changes in protocol and patient information / informed consent and asks to provide copy of final report.

Yours sincerely

11/6/14

Member secretary, Ethics Committee

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LIST OF ABBREVIATIONS

BMI	-	Body Mass Index
TGL	-	Triglycerides
LDL	-	Low Density Lipoprotein
HDL	-	High Density Lipoprotein
ANS	-	Autonomic Nervous system
ANFT	-	Autonomic Function Test
HRV	-	Heart Rate variability
WC	-	Waist Circumference
WHR	-	Waist Hip Ratio
AgRP	-	Agouti- related peptide
NPY	-	Neuropeptide Y
POMC	-	Pro-opiomelanocortin
CART	-	Cocaine –and amphetamine –regulated transcript.
FFA	-	Free Fatty Acids
VLDL	-	Very Low Density lipoprotein
SNS	-	Sympathetic Nervous System
PNS	-	Parasympathetic Nervous System
NTS	-	Nucleus Tractus Solitarius
RVLM	-	Rostral Ventrolateral Medulla
HR	-	Heart Rate
bpm	-	Beats per Minute
SBP	-	Systolic Blood Pressure
DBP	-	Diastolic Blood Pressure
PP	-	Pulse Pressure

MAP	-	Mean Arterial Pressure
NCEP	-	National Cholesterol Education Program
ATPIII	-	Adult Treatment Panel III
ECG	-	Electrocardiogram
PSD	-	Power spectral Density
DB	-	Deep breathing
RRI	-	RR interval
SD	-	Standard Deviation
SDNN	-	Standard Deviation of average Normal to Normal RR intervals
RMSSD	-	Root Mean of the Sum of Squares of Difference between adjacent Normal to Normal RR intervals
NN50	-	Normal to Normal RR interval deviation more than 50 ms
TP	-	Total Power
ms^2	-	Millisecond Square
LF	-	Low Frequency
HF	-	High Frequency
n.u.	-	Normalized units
VLF	-	Very Low frequency
ULF	-	Ultra Low Frequency

Background: Obesity is a major public health problem in developing countries. Obesity a state of excess adipose tissue mass is associated with number of cardiovascular disease and metabolic disturbances. Irrespective of etiology, Obesity is associated with autonomic dysfunction and contributes to obesity related comorbidities such ad insulin resistance, hypertension, dyslipidemia and cardiovascular dysfunction.

Aim and Objective: To compare lipid profile and autonomic function between obese and normal subjects and to assess the association of anthropometric indices and lipid profile parameters on autonomic function.

Materials and Methods: This study included 60 subjects in the age group of 25 – 40 years. BMI > 25 kg/m^2 were selected as study group. Age and sex matched, BMI of

18- 22.9 were selected as control group. Serum lipid profile estimation was done by enzymatic method. To assess autonomicfunction status, heart rate variability at supine rest, heart rate response to deep breathing, heart rate response to Valsalva maneuver and blood pressure response to isometric hand grip test were carried out. Data were collected by recording lead II ECGUsing physiopac pp8 medicated system. Short term HRV analysis was done using Kuopio's Finland version 2.2software. HRV parameters

Mean RR, SDNN, RMSSD, NN50, pNN50, Total power, LF nu, HF nu and LF /HF ratio were calculated.Maximum and Minimum RR interval was noted during Deep breathing and Valsalva maneuver. E/I ratio and Valsalva ratio were calculated. Blood pressure response to isometric hand grip exercise was measured using manual

sphygmomanometer. The correlation ofanthropometric indices and lipid profile parameterswith autonomic function test was also carried out.

Results: Unpaired student independent‘t’ test and spearman correlation coefficient was usedfor statistical analysis. Triglycerides, total cholesterol and LDL were significantly higher in obese group in comparison to control group whereas HDL was reduced in obese group. There was significant increase in the mean heart rate, LF nu and LF/HF ratio in obese group whereas Mean RR,SDNN, RMSSD, NN50, pNN50, total power. HFnu were significantly lower in obese group ($p<0.05$).E/I ratio and valsalva ratio were also significantly decreased in obese group compared to control($p<0.05$).Resting blood pressure was higher in obeseindividuals but in response to isometric hand grip was significantly lowered compared to control. Spearman’s correlation showed significant correlation of autonomic function with some anthropometricindices and lipid profile parameters.

Conclusion: The study demonstrates HRV indices indicating sympathetic activity were increased where those indicating parasympathetic activity were decreased. E/I ratio and valsalva ratio indicating the parasympathetic function were also reduced. The results suggestive of reduced parasympathetic activity associated with elevated sympathetic activity in obese males at rest.This sympathovagal imbalance makes them susceptible for development of cardiovascular disorders.

Keywords: Obesity, Lipid profile, Autonomic function and Heart rate variability.

INTRODUCTION

Obesity is a global epidemic which possess significant health hazard to human. It has been called as "New world syndrome"[1]. Obesity is defined by WHO as "abnormal or excessive collection of fat in the body to the extent that the health is impaired"[2] and further described that there is increasing trend in global epidemic of overweight and obesity as "Globesity"[3]. It is expressed in terms of body mass index (BMI). About 5% of Indian populations are morbid obese, emerging as a major health challenge. In India prevalence rises especially in urban areas followed by the urban slums and lower in rural populations[4].

Obesity a complex disease arising from interactions of genetic and environmental factors. It is associated with metabolic and cardiovascular diseases which is responsible for about 3 lakhs deaths in Asian population[5]. Obesity is also characterized by abnormal lipid profile of increase triglycerides (TGL), decrease high density lipoprotein (HDL) and increase low density lipoprotein (LDL) concentration which increases cardiovascular risk[6]. Apart from cardiovascular risk, the increase in prevalence of obesity predisposes to other co-morbidities including type 2 diabetes mellitus, autonomic dysfunction and certain cancer.

Autonomic nervous system (ANS) is involved in the control of cardiovascular system and energy metabolism by which it regulates bodyweight. Hypothalamus - regulatory center of satiety and of the ANS

becomes deranged, resulting in ANS dysfunction and obesity[1]. Obesity again has a great impact on the Autonomic nervous system in the form of increased sympathetic and decreased parasympathetic activity. Increased sympathetic activity leads to endothelial dysfunction, increase vasomotor tone, chronic low grade inflammation, hypertension and insulin resistance which acts as risk factors for cardiovascular dysfunction. Decreased parasympathetic activity increases heart rate and reduces Heart rate variability [5].

Autonomic dysfunction in combination with abnormal lipid profile in obesity promotes inflammation, oxidative stress and atherosclerosis and lowers threshold for ventricular arrhythmia which increases risk of sudden cardiac death. As per Framingham Heart study, in obese men the incidence of cardiac failure leading to sudden death is more common[7]. So this study is carried out in obese male individuals.

Hence the aim of this study is to evaluate the cardiovascular risk factors in obese male individuals based on their lipid profile status and cardiovascular autonomic function tests (AFT). AFT includes Resting Heart rate variability (HRV), Heart rate changes during one minute controlled deep breathing (DBT), Valsalva maneuver (VM) and Sustained isometric hand grip test (SIHG). HRV is the physiological phenomenon of variation in the time interval between heart beats. It reflects the activity of sympathetic and parasympathetic system on sinus node of the heart and reduced HRV implies autonomic imbalance.

OBESITY

Hippocrates noted “sudden death is more common in those who are naturally fat than in the lean”.

Galen et al elaborated on different degrees of obesity as moderate or common obesity and severe or morbid obesity[8].

Obesity an excessive accumulation of body fat results in generalized increase in body mass index. BMI is derived by Quetelet’s index as weight in kilograms divided by the square of the height [weight (kg)/height (m^2)] [2]. It is related to body fat percentage and total body fat. It is the most useful method to estimate prevalence of obesity in a population level. Because of association between BMI and adiposity it has been internationally accepted to assess weight related health risk [9].

ASIAN PACIFIC GUIDELINES FOR OBESITY (BMI in Kg/m^2)[4], [10]

As per the guidelines, Obesity is classified as follows,

- Underweight < 18.5 has low risk for co-morbidities
- Normal weight 18.5-22.9 has average risk for co-morbidities
- Overweight: ≥ 23, further classified as
- At risk for obesity 23-24.9 has increased risk for comorbidities
- Obese I 25-29.9 has moderate risk for comorbidities
- Obese II ≥ 30 has severe risk for co-morbidities.

BMI Cut-offs of obesity for Adult Europids in (kg/m^2)[10]:

As per this, the criteria for obesity

- Underweight <18.5 with low risk for co-morbidities.
- Normal weight18.5-24.9 with average risk for co-morbidities.
- Over weight ≥25 is further classified as
- Pre obese 25-29.9 with increased risk for comorbidities
- Obese I 30-34.9 with moderate risk for co-morbidities
- Obese II 35-39.9 with severe risk for co-morbidities
- Obese III ≥40 with very severe risk for co-morbidities

Other classification of obesity

Based on distribution of fats, obesity is classified as

Central or Android Obesity:

They are more risk for cardiovascular and metabolic complications and it is common in men.

Peripheral or Gynecoid Obesity:

They are less risk for cardiovascular and metabolic complications and it is common in women[4].

South Asian trait of people has higher percentage of body fat and increased cardiovascular risk at lower BMI compared with Caucasian population[11]. Asian cutoff of BMI for overweight is ≥23 kg/m^2 and obesity is≥25kg/m^2. The present study was conducted based on Asian pacific guidelines for obesity[4, 10].

South Asians has more centralized distribution of fat and high prevalence of abdominal obesity. Previous studies have proposed that waist circumference (WC) as well as waist hip ratio (WHR) estimates the abdominal obesity and cardiovascular risk[12]. **Hence in this study, WC and WHR are compared between obese and normal groups.** However preferred measure of abdominal obesity is WC compared with WHR ratio[10].

Waist circumference cut off values of abdominal obesity for

Asian male and female is 90 cm and 80cm[11].

ETIOPATHOGENESIS OF OBESITY

Obesity is due to imbalance between one's energy intake and energy expenditure.

Energy intake

A complex physiological system integrates signals from peripheral organ to brain to control energy intake and energy expenditure. Signals may be neural, metabolic and hormonal.

Food intake is influenced by factors integrated in the Hypothalamic Arcuate nucleus (ARH). There is a balance between interactions of two sets of neurons in hypothalamus.

Neurons secreting Agouti- related peptides (AgRP) and Neuropeptide Y (NPY) that increases food intake and reduces energy expenditure.

Neurons secreting Pro-opiomelanocortin (POMC) and Cocaine-and amphetamine-regulated transcripts (CART) that decreases food intake and increases energy expenditure[13].

Neural signals concerned with satiety reach the brainstem and controls food intake. Metabolic signals like decrease plasma concentrations of glucose, amino acids and fatty acids stimulate food intake by interacting with nervous system. This is known as Glucostatic theory of hunger and feeding regulation, aminostatic and lipostatic theories of regulation. When blood sugar level rises, discharge rate of glucoreceptor neuron in the satiety center of ventromedial nuclei of hypothalamus increases but discharge rate of glucosensitive neuron in the hunger center of lateral hypothalamic nuclei decreases. Nutrients also stimulate the release of hormones that controls food intake[14].

Role of adipokines

There are many biologically active substances secreted by the adipose tissue called adipokines like Leptin, Resistin, Adiponectin, Free fatty acids, TNF alpha, IL-6 etc. Of all hormonal signals, secreted from adipose tissue, Leptin regulates energy intake by acting on arcuate nucleus of hypothalamus. It also regulates energy expenditure by sympathetic nervous system

stimulation. Leptin decreases the food intake by stimulating POMC and α-MSH formation and by inhibiting the expression of NPY and Ag RP[13, 14]. **Leptin resistance in satiety center of hypothalamus** is a proposed mechanism for obesity as it increases food intake, thereby resulting in a vicious cycle[6, 15].

Other hormones participating in regulation of food intake include, Insulin secreted by pancreas which binds to receptors in arcuate nucleus of hypothalamus decreases food intake by stimulating leptin release. CCK secreted from small intestine acts rapidly and decreases food intake. Peptide YY secreted from GIT decreases the appetite. Corticotrophin releasing hormone, nor epinephrine and serotonin also decreases food intake. Ghrelin an endogenous ligand of growth hormone secretagogue released by gastrointestinal tract stimulates food intake and carbohydrate utilization. Orexin A and B, Endorphins, Melanin concentrating hormone (MCH), Amino acids (glutamate and γ -amino butyric acid), Galanin (GAL), Cortisol and Endocannabinoids increases food intake. Obestatin and ghrelin, synthesized from same precursor protein have opposite effect. Obestatin decreases food intake whereas ghrelin increases food intake[16].

Energy Expenditure

It includes basal metabolic rate, energy cost of metabolizing food during physical activity and adaptive thermogenesis. Resting or Basal metabolic rate accounts for 70% whereas physical activity for 5-10 % of daily energy expenditure[13]. Thus the significant component of consumption of energy is fixed. During sleep it falls about 10% and during prolonged

starvation up to 40%[17]. Adaptive thermogenesis occurs in brown adipose tissue. This process produces more heat and less ATP by utilizing mitochondrial uncoupling protein (UCP-1) that uncouples oxidative phosphorylation from electron transport and is regulated by sympathetic activity.

Genetic Factors

Genetics plays role in body weight regulation by regulating energy expenditure, thus 30-40% variance in daily energy expenditure is influenced by genotype[18]. Certain genetic background individuals are prone for obesity especially when exposed to modern lifestyle. Genetic contribution to obesity has shown in Twin studies, adoption studies and family studies[19].

Genetic studies in mice demonstrated obesity due to mutation of at least 5 identified genes – ob (obesity) gene encoding Leptin, db (diabetes) gene, tubby, agouti yellow and fat genes. In ob/ob mice, leptin gene is defect and in db/db mouse leptin receptor are defect. In majority of obese population leptin resistance might be one of the main reasons for obesity, though they have normal leptin and leptin receptor[20].

Severe obesity commencing in childhood without developmental abnormalities are due to mutations arising in molecule involved in Leptin–Melanocortin signaling pathway. Such as Leptin gene mutation [lepob)], Leptin receptor gene mutation [lepR(db)], Pro-opiomelanocortin gene mutation (POMC), Prohormone convertase 1 gene mutation (PCSK1) and Melanocortin 4 receptor gene mutation (MC4R)[13]. There are about 30

Mendelian disorders in which obesity is associated with developmental abnormalities, like mental retardation, dysmorphic features. They are Prader-Willi Syndrome, Bardet-Biedl Syndrome, Fragile X syndrome, Cohen's syndrome, Albright Hereditary Osteodystrophy and BDNF/TrKB deficiency. Endocrine disorders like Cushing syndrome, polycystic ovarian disorder and some drugs like Anticonvulsants, Anti-hypertensive drugs are also associated with obesity.

Environmental factors

Although genetics influences the body weight regulation[21], Current obesity epidemics is result of environmental and behavioral factors interacting with genetic susceptibility[22]. Incidence of obesity increases due to "Obesogenic" environment that promote overeating, easy availability of palatable energy dense foods together with reduced energy expenditure[23]. WHO Consultation on Obesity concluded that behavior and environmental factors play a major role for the past two decades[9].

LIPID METABOLISM

Exogenous Pathway

Dietary lipids are absorbed in small intestine as chylomicrons. Lipoprotein lipase (LPL) hydrolyses the triglycerides of chylomicrons to release free fatty acids (FFA). The free fatty acids released are oxidized in the muscles or adipose tissue to produce energy. It is also stored as triglycerides by re-esterification.

Endogenous Pathway

Fatty acids released by lipolysis of adipose tissue are reassembled in the liver as Very low density lipoprotein (VLDL) which is secreted into the plasma. VLDL are metabolized by lipoprotein lipase to form IDL and converted into LDL by hepatic lipase.

HDL Metabolism

To maintain homeostasis liver excretes excess cholesterol as bile. Liver and intestine produces nascent HDL. Nascent HDL acquires free cholesterol from peripheral tissue and gets esterified by Lecithin cholesterol acyltransferase forming mature HDL. Cholesterol from mature HDL is transferred to VLDL and chylomicrons by cholesterol ester transfer protein and then back to liver.

Role of Adipose Tissue in Lipid Metabolism-Triglyceride storage and lipolysis

Adipose tissue is the energy storage organ. Exogenous dietary lipids called chylomicrons and endogenous VLDL are acted by lipoprotein lipase to release free fatty acids, which are stored as triglycerides in adipose tissue. Hormone sensitive lipase (HSL) hydrolyzes triglycerides into fatty acids for energy. Thus there is a balance between triglyceride storage and lipolysis generally which is influenced by complex hormonal and neuronal mechanism. Rate of lipolysis and level of fatty acids in plasma varies within and between subjects which is due to dose response effect of insulin and catecholamine on lipolysis and absence of feedback regulation of insulin and catecholamine

level by free fatty acids. Insulin and catecholamine are major hormones that influence lipolysis. Insulin inhibits lipolysis through its effect on hormone sensitive lipase whereas catecholamine stimulates lipolysis. In extremely obese adult's adipocyte mass increases about four times with lipid content about twice [11].

Effect of obesity on Lipid Metabolism

In obese individuals, basal fatty acids concentration increases because expanded adipose tissue releases more FFA or FFA clearance is reduced [11]. In abdominal obesity, visceral fat shows less sensitivity to anti-lipolytic effect of insulin and more sensitivity to lipolytic effect of catecholamine, so it stimulate lipolysis via beta-3 receptor. The excess free fatty acids in plasma increases hepatic uptake and triglyceride rich VLDL synthesis. Also decrease LPL activity associated with insulin resistance slows down the normal clearance of VLDL[24]. Thus increased triglyceride rich VLDL in liver favours exchange of triglycerides and cholesterol ester between VLDL, HDL and LDL such that triglyceride rich HDL particles are formed which are rapidly hydrolyzed and cleared.

In hypertriglyceridemia, cholesterol ester transfer protein reduces the cholesterol-ester concentration of LDL and increases the triglyceride concentration of LDL. The elevated triglyceride concentration within the LDL is acted upon by hepatic lipase, which results in the formation of small dense LDL particles[25]. Small dense LDL is more prone for oxidation due to decreased free cholesterol. Small dense LDL is slowly metabolized and plays a major role in the development of atherosclerosis and cardiovascular disease.

Obesity with such abnormal lipid profile of increase in triglycerides, decrease in HDL and abnormal small LDL increases the cardiovascular risk[26, 27]. Hence, we intended to evaluate the synergistic risk of obesity with abnormal lipid profile in this study.

Obesity and Metabolic syndrome

The adipose tissue acts as the culprit in insulin resistance and metabolic syndrome. Among the adipokines, Leptin, Adiponectin, Resistin, TNF alpha and RBP2 has great effect on insulin resistance. With excess fat mass, leptin increases and suppresses insulin production. Adiponectin increases insulin sensitivity. When plasma concentration of adiponectin decreases in obesity, insulin resistance occurs. Resistin, Retinol binding protein 2, TNF alpha and IL-6 also increases in obesity and contributes to insulin resistance[11]. Hyperinsulinemia as result of insulin resistance in obesity, acts on sympathetic nervous system contributes to hypertension and further adverse consequences.

Criteria for Clinical Diagnosis of Metabolic Syndrome:

1. Abdominal obesity (WC≥90 cm for Asian male or ≥80 cm for Asian female),
2. Triglycerides more than or equal to 150 mg/dl,
3. HDL cholesterol less than or equal to 40 mg/dl for male and 50 mg/dl for female,
4. Systolic/diastolic blood pressure more than or equal to 130/85 mmHg and
5. Fasting plasma glucose more than or equal to 100 mg/dl.

As per Revised National Cholesterol Education program Adult Treatment Panel III ((NCEP ATP III) criteria at least three of the following components are required for diagnosis of metabolic syndrome. Abdominal obesity is not a prerequisite for diagnosis, [28] but a component of the metabolic syndrome.

AUTONOMIC NERVOUS SYSTEM

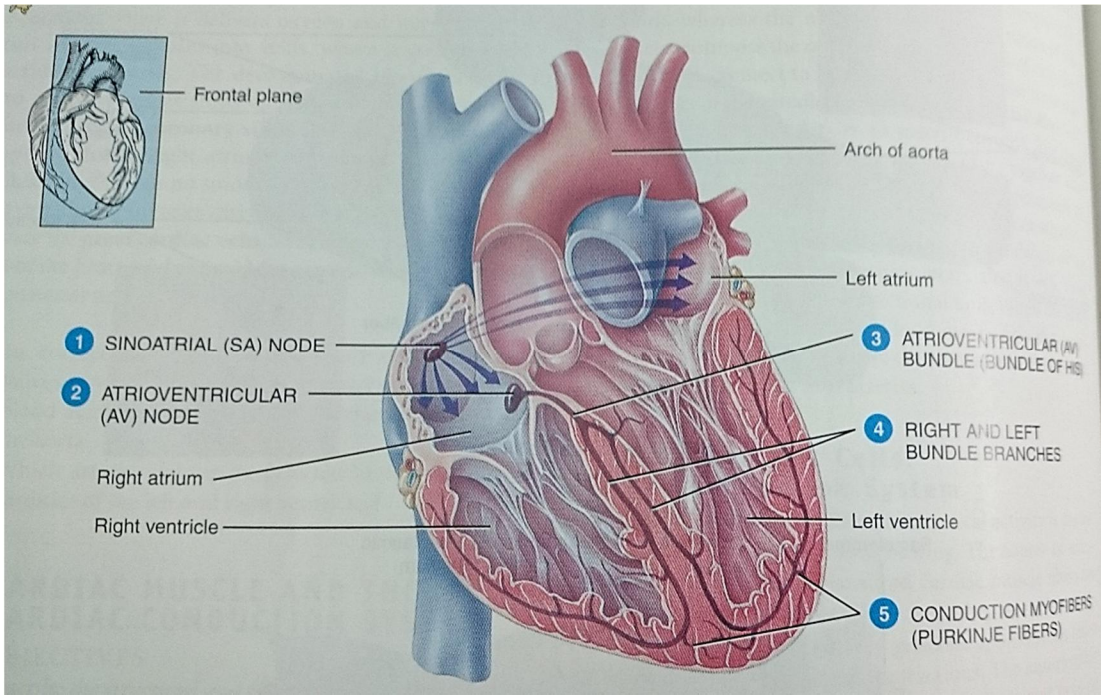
The term "Autonomic nervous system" was proposed by Langley (1852-1925)[29]. It is a peripheral nervous system that controls heart rate, arterial pressure, respiratory rate, GI secretions and motility, sweating, body temperature, pupillary dilation, bladder emptying and sexual arousing. Though ANS functions autonomously, it is also influenced by higher center especially the hypothalamus and medulla oblongata that receive inputs from the limbic system and other cortical regions [14]. ANS response is mediated by sympathetic and parasympathetic division. Sympathetic nervous system (SNS) predominates in energy mobilization and utilization and the parasympathetic nervous system (PNS) in energy restoration and storage. Thoracic-lumbar outflow T1-L2 is considered to be sympathetic and cranio-sacral outflow is considered to be parasympathetic[30]. All preganglionic fibers are cholinergic in both sympathetic and parasympathetic system whereas most of the postganglionic sympathetic neurons are adrenergic and most of the postganglionic parasympathetic neurons are cholinergic. However postganglionic sympathetic fibers to the piloerector muscles of the hairs, to the sweat glands and some skeletal muscle blood vessels are cholinergic[17].

Autonomic Innervation and action on the Heart and Blood Vessels

Heart has drawn its sympathetic innervations from neurons in the intermediolateral horn of upper five thoracic segments of spinal cord. It innervates cardiac muscle tissue mainly atrial and ventricles. Noradrenaline from sympathetic nerve acts via beta1 adrenergic receptor by increasing calcium conductance decreases the threshold of firing of sinoatrial node and increases the heart rate. Parasympathetic originates from medulla in Dorsal motor nucleus and Nucleus Ambiguus innervates myocardial tissue predominantly sinoatrial node, atrioventricular node and conducting system. Acetylcholine from parasympathetic nerve acts via M2 muscarinic receptor by increasing the potassium influx increases the threshold of sinoatrial node firing and decreases the heart rate [17].

Normally, at rest there is good tonic vagal discharge (vagal tone) and moderate amount of sympathetic discharge to heart. Noradrenergic sympathetic fibers innervate blood vessels. Neurotransmitters such as Noradrenaline predominantly acts via alpha1 receptors mediate vasoconstriction whereas Adrenaline mediates its action via both alpha and beta 2adrenergic receptors with predominate vasodilation. Thus sympathetic plays a role in circulation whereas parasympathetic in cardiac functions.

FIGURE: 1 CONDUCTING SYSTEM OF HEART



Brain centers for cardiovascular regulations:

Sensory Nucleus for Autonomic nervous system is Nucleus of the tractus solitarius (NTS) located bilaterally in lateral portion of the medulla is the first relay station which receives sensory information from circulatory system via glossopharyngeal and vagus nerve modify the activities of both cardiovascular excitatory area and cardiovascular inhibitory area. Cardiovascular excitatory area is in rostral ventrolateral medulla (RVLM). Neurons in this area project to intermediolateral grey column of spinal cord where sympathetic vasoconstrictor fibers originates. It is important to note that neurons in this area (RVLM) provide excitatory drive to vasoconstrictor fibers to maintain basal sympathetic tone of blood vessels. Cardiovascular inhibitory area is in Nucleus Ambiguus and Dorsal motor nucleus of vagus in medulla

transmits parasympathetic impulse to heart, decrease heart rate and ventricular contraction[31].

Effect of obesity on Autonomic nervous system

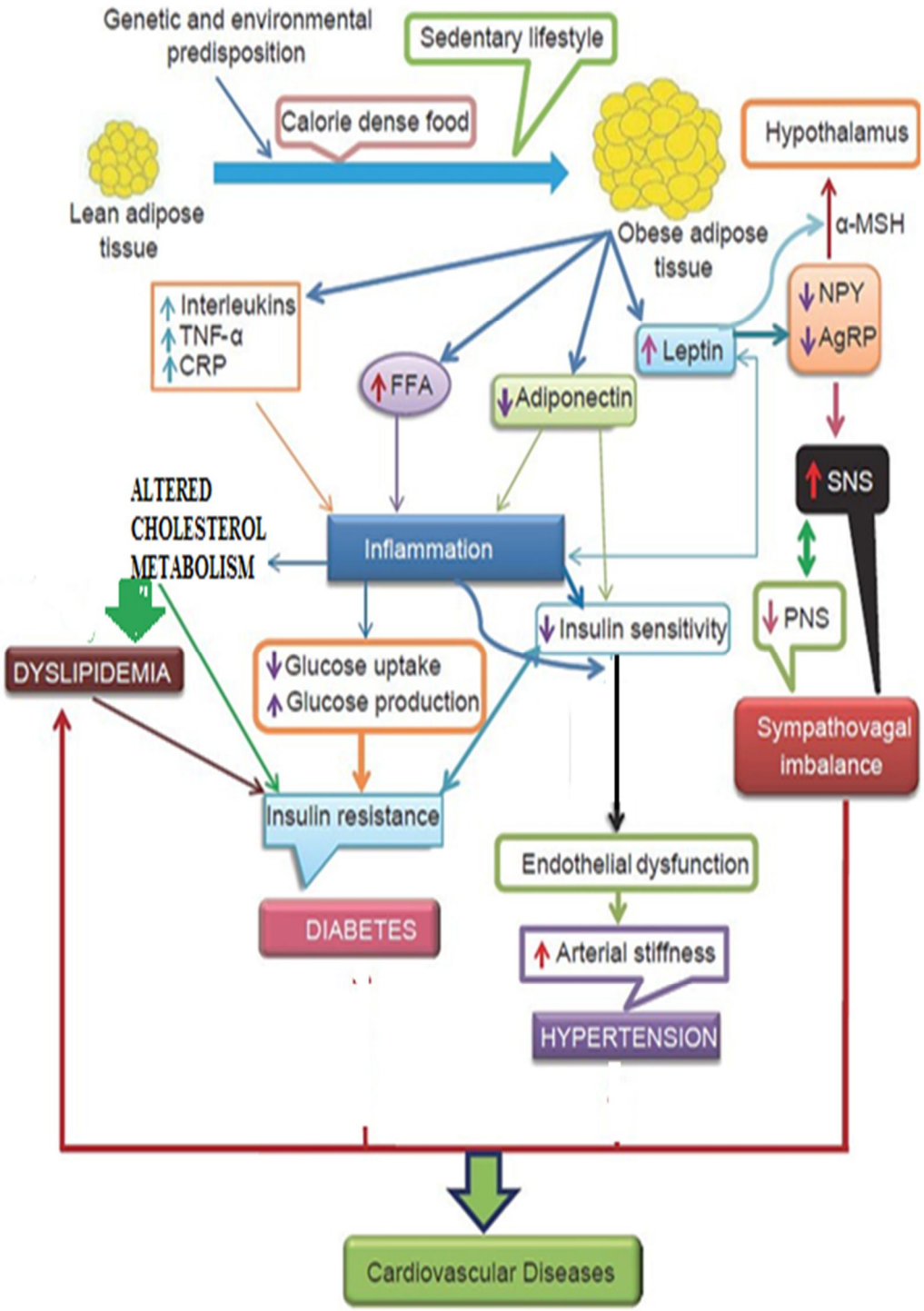
In obese individuals, the function of autonomic nervous system is commonly altered. There is increased oxidative stress in obesity which decreases insulin sensitivity thereby increases the circulating insulin level and the sympathetic activity. Landsberg[32] et al originally postulated that enhanced autonomic activity in obesity is related to high insulin level, as it acts directly on hypothalamus to activate sympathetic nervous system[33]. Adipose tissue in excess releases excess leptin in obese, activates central sympathetic flow and further it increases adrenal medullary release of noradrenaline and its activity[34, 35].

Obesity is an inflammatory state it produces cytokines like 8-isoprostane, IL-12, IL-6, CRP and TNF-α stimulates hypothalamic pituitary adrenal axis to release glucocorticoids and adrenaline which in turn increases the sympathetic nervous system activity[36,37]. Hyperinsulinemia (or) insulin resistance also causes damage to microcirculation in many tissue including nerves at level of cardiac muscle or vascular wall resulting in parasympathetic impairment[38]. This increased sympathetic activity and decreased parasympathetic activity are associated with attenuation of baroreflex response in obesity. Baroreflex response is influenced by BMI, age, autonomic nervous system and arterial distensibility. In obesity, decreased arterial wall compliance due to atherosclerosis also reduces baroreflex response [39].

Factors causing increase cardiovascular risk in obesity

In obesity, increase sympathetic activity, through β-adrenergic stimulatory and vasoconstrictor effect causes reduction in muscular blood flow contribute to insulin resistance. Insulin resistance and hyperleptinemia in obesity down regulate endothelial NO synthase whereas hyperinsulinemia upregulate endothelin-1activity cause hypertension and further consequences in obesity. Adipocytokines from adipose tissue regulate the synthesis of pro-inflammatory cytokines leptin, TNF-α, IL-6 and anti-inflammatory cytokines adiponectin and resistin. In obesity there is imbalance between two, increases cardiovascular risk. CRP is a marker of inflammatory state and endothelial dysfunction is found to be increased in obese individuals[40]. IL-6 increases in proportion to body fat and stimulates prothrombotic events[36]. Thus Hyperglycemia, Hypertension, Coagulation defects and Dyslipidemia increases the risk of coronary artery disease.

FIGURE: 2 RISK FACTORS OF CARDIOVASCULAR DISEASE IN OBESITY



CARDIOVASCULAR AUTONOMIC FUNCTION TESTS

In Previous studies, sympathetic nervous system activity is assessed by measuring plasma and urinary catecholamine concentration[41]. Muscle nerve sympathetic activity is recorded using microneurography (MNSA). But has limitations as sympathetic out flow to skeletal muscle may not reflect sympathetic activity in other organs such as the heart and kidneys. In 1970s, Ewing et al[42,43] proposed a reliable, non-invasive, simple bedside Cardiovascular autonomic function test to diagnose as well as monitor autonomic nerve involvement. Mostly they rely on cardiovascular changes such as Heart rate (HR) and Blood pressure (BP) response to postural changes, carotid sinus massage, heart rate variation to deep breathing and valsalva maneuver, sustained isometric hand grip and cold pressor test.

Parasympathetic function test are

Heart rate response to Standing: (30:15ratio)

On standing heart rate increases and reaches its maximum at 15th beat (approximately 12 seconds) due to vagal withdrawal and increase sympathetic tone and it progressively slows down reaches minimum at 30th beat (approximately 20 seconds) after standing and then it gradually rises again. The ratio of maximum R-R intervals corresponding to the 30^{th} beat and the minimum RR intervals corresponding to the 15^{th} beat is called 30:15ratio. i.e., RRmax30/RRmin15 [44].

Heart rate changes during one minute controlled deep breathing

Normally heart rate varies from beat to beat as vagal activity synchronous with the respiratory cycle (Respiratory sinus arrhythmia). At inspiration, vagal withdrawal and increased venous return stretch atrial receptors to produce tachycardia. Conversely at expiration, vagal activity and decreased venous return reduces heart rate. It asses the cardiac vagal activity and it is influenced by age, rate and depth of respiration[44].

$$\text{Expiration/inspiration:} \quad \frac{\text{longest R-R during expiration}}{\text{shortest R-R during inspiration}}$$

Heart rate changes during Valsalva maneuver

It is performed by exhaling forcefully through a mouth piece connected to a mercury manometer for 15 or 20 seconds with mercury column maintained at 40mmHg. Hemodynamic changes in Valsalva maneuver divided into 4 phases as

During phase I, at the onset of straining, arterial pressure rises transiently due to compression of the aorta and is accompanied by reflex decrease in heart rate.

During early part of the phase II, (at expiratory phase of the Valsalva maneuver) as the subject blows forcefully through the mouthpiece against resistance, intrathoracic pressure raises and venous return, cardiac output and arterial pressure falls accompanied by increase in heart rate due to parasympathetic withdrawal and increased sympathetic outflow. In the latter

part, after few seconds arterial pressure begins to recover and rise above baseline.

During phase III, on the cessation of straining intrathoracic pressure falls and pulmonary venous capacitance raises, arterial pressure decreases further accompanied by a reflex increase in heart rate.

During Phase IV with further release of strain there is an increase in arterial pressure above the base line i.e., overshoots due to increase in venous return and cardiac output. It is accompanied by reflex bradycardia followed by a gradual return of heart rate to base line as blood pressure normalizes. The bradycardia in this phase is vagaly mediated.

Thus Phase I and III are due to mechanical factors. Phase II and IV are the consequence of sympathetic, vagal and baroreflex mechanism[45].

$$\text{Valsalva ratio: } \frac{\text{Maximum RR interval during phase IV}}{\text{Minimum RR interval during phase II.}}$$

Tests for sympathetic function

Blood pressure response to Standing (Orthostatic tolerance test)

Measure blood pressure using sphygmomanometer manually in the lying position and then ask the subject to stand then repeat BP measurement immediately. Difference of the systolic blood pressure was calculated, a fall of systolic BP more than 30 mmHg is abnormal[43].

Blood pressure response to Valsalva maneuver

Beat to beat blood pressure was recorded during Valsalva maneuver. Sympathetic failure is characterized by profound decrease of BP in phase II and an absence of blood pressure overshoot in phase IV of Valsalva maneuver[45].

Cold pressor test (CPT)

While hand or foot is immersed in ice water there is reflex arteriolar vasoconstriction produces rise in arterial pressure triggered by cutaneous pain receptors. Blood pressure rises mainly due to enhanced sympathetic activity and increase vascular resistance[45].

Sustained isometric hand grip test (SIHG)

The pressor response to the isometric exercise is mediated by central command and exercising muscles. There is increase sympathetic discharge to the heart and muscle during exercise. This causes peripheral vasoconstriction in some non-contracting tissue and heart rate dependent increase in cardiac output and blood pressure[44].

HRV BACK GROUND (Task Force 1996)[46]

Besides this conventional autonomic function test, Heart rate variability acts as a noninvasive tool to assess cardiovascular autonomic function. HRV refers to the oscillation in the interval between consecutive heartbeats as well as the oscillation between consecutive instantaneous hear rate. It reflects the sympathetic and parasympathetic activity on sinus node of the heart and

instantaneous HR or RR interval is the sum of these inputs. HRV analysis is performed under linear methods in time domain and frequency domain methods.

Time domain methods

In this method, LEADII ECG is recorded continuously, each QRS complex is detected and normal-normal (NN) intervals, the intervals between adjacent normal QRS complex (or) instantaneous heart rate are determined.

SDNN: the standard deviation of normal-normal intervals. It is often calculated over a 24 hour period, **express parasympathetic activity.**

SDANN: the standard deviation of the average normal-normal intervals calculated over short periods usually 5 minutes.

RMSSD: the square root of the mean squared differences of adjacent NN intervals.

NN50: the number of pairs of successive NN intervals that differ by greater than 50ms.

pNN50: Proportion of NN50 divided by total number of NN intervals

Frequency Domain Methods

In Short term recordings of about 5 minutes, Frequency domains methods are generally done and following components have been defined:-

- Low frequency component (LF) between 0.04 and 0.15Hz

Indicates mainly sympathetic activity or combination of both sympathetic and parasympathetic activity

- High frequency component (HF) between 0.15and 0.4Hz

Reflects parasympathetic activity, oscillations depend primarily on respiration.

- Very low frequency component (VLF) between 0.0033 and 0.04Hz

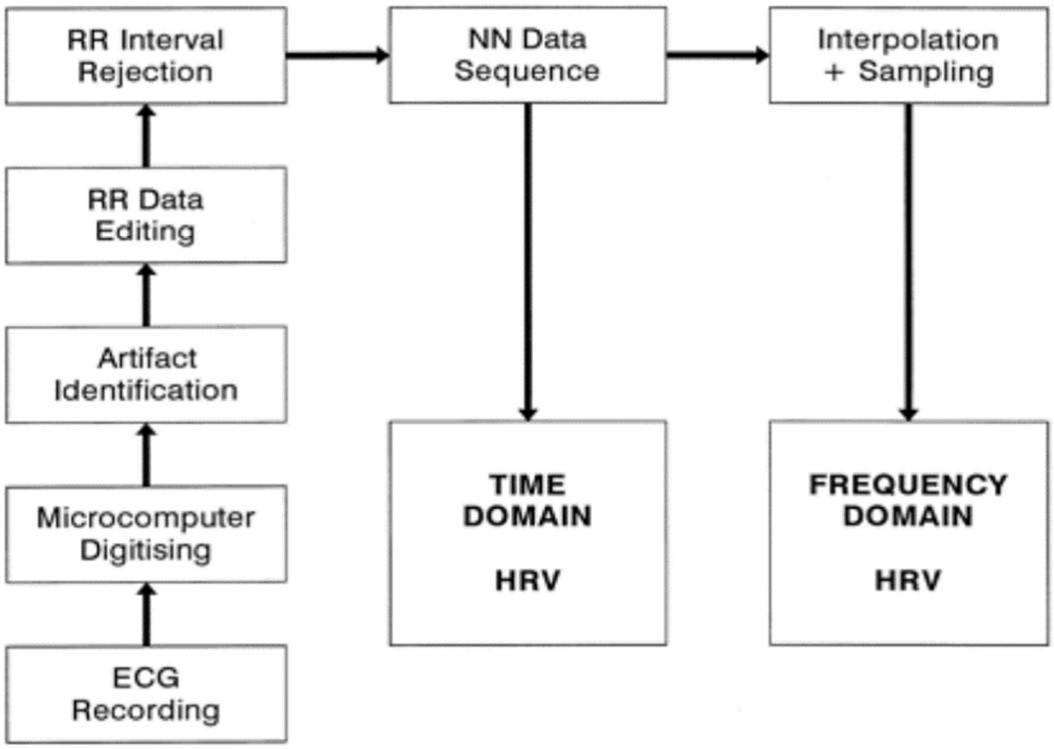
Whose origin is not clear it may be due to thermal regulation of body's internal systems.

- Ultra-low frequency component (ULF) between 0 and 0.0033Hz is always expressed in 24hrs recording and show day-night variations.

LF-HF ratio:

It is the ratio of low-to-high frequency spectral power reflects sympathovagal balance. This is controversial due to lack of understanding of the mechanisms for the LF component. The measurement of VLF, LF and HF power components usually made in absolute values of power (milliseconds squared). LF and HF measured in normalized units may represent the relative value of each power component in proportion to the total power minus VLF component. Total power is the ultimate measure in power spectral density, an indicator of autonomic modulation as a whole.

FIGURE: 3 GENESIS OF HRV



Recording requirements

ECG Signal

Fiducial point of the QRS complex of the Lead II ECG is identified based on the maximum or baricentrum of the complex. It is difficult to identify the QRS complex fiducial point if an upper-band frequency cutoff is lower than the established frequency band for diagnostic equipment (200Hz) and this may introduce an error in measured RR intervals. Error introduced in HRV spectrum due to limited sampling rate can be decreased by interpolation of the under sampled ECG signal. Hence, when there is an appropriate interpolation even 100 Hz sampling rate will be adequate.

REVIEW OF LITERATURE

- 1528, Galen showed sympathovagal trunk
- 1898, Langley introduced Autonomic nervous system.
- 1920, Hering found the existence of Baroreflex activity
- 1948, Alquist found the receptors and Sympathetic nervous system.
- 1966, Albert B Lewin observed heart rate changes during Valsalva maneuver.
- 1965, Hon and Lee first recognized the clinical relevance of HRV when they noted the fetal heart rate changes during fetal distress.
- 1970, Ewing and Clark devised simple noninvasive tests using cardiovascular tests to assess autonomic dysfunction.

Jong Weon Choi1et al (2002)[47] investigated relationship between anthropometric parameters, total body fat and serum lipid profile and reported that correlation between serum lipid profile and total body fat were better than BMI.

Walton C et al (1995)[48] observed that fat distribution is highly associated with elevated total serum triglycerides and decreased HDL.

Stephen R et al (1999)[49] Studied that fat distribution has significant correlation with cardiovascular risk factors than percent body fats, particularly android fat distribution.

Savva1 et al (2000) [50] validated that waist height ratio and waist circumference are good predictors of cardiovascular risk than BMI.

Guenther Boden et al (2008)[51] evidenced that free fatty acids causes both insulin resistance and inflammation, a link for the development of risk component for atherosclerotic vascular disease such as type II diabetes mellitus, hypertension, atherogenic dyslipidemia and disorders of blood coagulation .

Carey N. Lumeng et al (2011)[52] evaluated the role of inflammation in the obesity complication and reframed obesity as an inflammatory condition, which had a wide impact on obesity associated diseases.

Zohreh mazloom et al (2009)[53] noted that obese women had significantly higher serum concentrations of CRP, triglycerides and cholesterol compared to non-obese.

Luisa Soares et al (2011)[54] studied in obese and overweight girls the relationship between central fat and cardiovascular autonomic function and reported that increased central fat is associated with parasympathetic hypoactivity and sympathetic hyperactivity, independent of the total body fat.

Aronel J et al (1995)[55] supported that in non-obese subjects, 10% weight gain causes sympathetic over activity and reduced parasympathetic

activity. Conversely weight loss of 10% results decreased sympathetic and increased parasympathetic activity and thus the autonomic nervous system act to oppose weight change.

Bernd Fruehwald et al (1999)[56] demonstrated an acute stimulation of hypothalamus pituitary adrenal axis by supraphysiological level of insulin in abdominal obese.

Scherrer U et al (1994)[57] observed a relationship between fasting plasma insulin concentration and sympathetic firing rate positively and hypothesized that sympathetic activation in overweight persons is due to hyperinsulinemia and further supported it by infusing low dose of insulin in lean person causes marked sympathetic activation.

Mariovaz et al (1997)[58] studied sympathetic nervous system function by regional sympathetic nervous system activity as plasma or urinary norepinephrine is unable to define sympathetic nervous system function in obesity. They investigated sympathetic nerve activity in kidney, heart and hepatomesentric bed and concluded that regional sympathetic nervous system activity was heterogeneous, higher renal norepinephrine spill overrate in obesity have implicated in the development of hypertension

Kazuko Masuo et al (2000)[59] evaluated the mechanism of blood pressure elevation in weight gain based on fasting plasma insulin, leptin and sympathetic nervous system then reported that sympathetic overactivity in weight gain is more likely associated with weight gain induced arterial

pressure elevation than the changes in leptin and insulin level of plasma that accompanies weight gain.

Shahin Akhter et al (2010)[60] conducted a study in age and sex matched 40 obese and non-obese individuals, 5 noninvasive cardiovascular test-Valsalva ratio, heart rate changes to deep breathing, heart rate changes to standing showed significantly lower value in obese subjects which indicates decreased parasympathetic nerve function and also baroreflex sensitivity. Arterial pressure response to isometric hand grip exercise shows lesser rise of DBP and Blood pressure response to standing from lying showed greater fall of SBP which indicates decreased sympathetic activity.

Chin HuaFu et al (2008)[61]found negative correlation between baroreflex sensitivity and LDL cholesterol. It is due to impaired endothelium dependent arterial dilatation in vessel wall caused by higher lipid profile which changes the baroreflex capacity.

M.Bootsma et al (1994)[62] demonstrated linear relationship between LF and HR and thus emphasized the significance of heart rate variability as a non-invasive method of assessing sympathovagal balance.

HayanoJ et al (1991)[63] reported that most of the time and frequency domain analysis provides an accurate and common measure of cardiac vagal tone at rest.

Piccirillo G (1998)[64] reported that obese have increased sympathetic arterial pressure variation with decreased heart rate variation , due to high

plasma noradrenaline level and found low LF power of heart rate as a result of diminished adrenoceptor responsiveness.

Michikazu Sekine et a (2001)[65] determined relationship between obesity and cardiac autonomic activity in 16 healthy male children 9 non-obese and 7 obese, reported lower TP and HF nu reflecting decreased cardiac parasympathetic activity and increase LF nu and LHR reflecting increased cardiac sympathetic activity.

AIM AND OBJECTIVE

AIM

To Evaluate the Lipid profile and Cardiovascular Autonomic Functions in obese male individuals.

OBJECTIVE OF THE STUDY

To compare the lipid profile and cardiovascular autonomic function changes between two groups (obese male and non-obese male group).

To assess the impact of anthropometric indices and lipid profile parameters on cardiovascular autonomic functions.

Using standard cardiovascular autonomic function test includes

1. Heart rate variability at supine rest.
2. Heart rate changes during one minute controlled deep breathing.
3. Heart rate response to Valsalva maneuver
4. Blood pressure response to Sustained isometric hand grip test.

MATERIALS AND METHODS

STUDY GROUP

The study group was obese male individuals without any gross systemic disease of BMI $\geq$ 25 kg/m^2 attending master health checkup OPD, Chengalpattu Medical College and Hospital, Chengalpattu.

Subjects were explained about the procedure. Informed and written consent was obtained from them.

INCLUSION CRITERIA

BMI $\geq$ 25 kg/m^2 based on Asian pacific guidelines.

Males of age group between 25-40 years were included.

EXCLUSION CRITERIA

Patient with Comorbid cardiovascular diseases such as ischemic heart disease, cerebrovascular disease.

Known diabetes mellitus, hypertension, lung disease and nephropathy.

Known smoker or alcoholic.

On any drugs affecting the autonomic function.

ANTHROPOMETRIC MEASUREMENTS

Weight, height, waist circumference (WC) and hip circumference (HC) were measured in cm. The BMI (using Quetelet's index) and waist hip ratio were calculated.

BODY WEIGHT

Body weight was measured without shoes with an accuracy of ±10gm using human adult calibrated weighing machine scale.

HEIGHT

Stadiometer was used to measure standard body height to the nearest 0.5 cm without shoes with relaxing the shoulder and hanging the arms freely.

BODY MASS INDEX

BMI was calculated by Quetelet's index as weight in kilograms divided by the square of the height in meter square [weight (kg)/height (m^2)]

WAIST CIRCUMFERENCE

At the level of midpoint between the lower rib and iliac crest, Waist circumference was measured using measuring inch tape in cm.

HIP CIRCUMFERENCE

At the greatest diameter at the buttock, Hip circumference was measured using measuring inch tape in cm.

WAIST HIP RATIO

By dividing waist circumference and hip circumference, WHR was calculated

CONTROLS

Healthy normal volunteers, age and sex matched, BMI between ≥ 18.5-22.9 kg/m^2 attending Master Health Check- up OPD, Chengalpattu Medical College and Hospital, Chengalpattu.

STUDY DESIGN

Case control study.

EXPERIMENTAL PROTOCOL

Fasting blood sample was drawn to estimate sugar by calorimetric enzymatic method. Fasting plasma glucose ≥ 126mg/dl were excluded[66]. On the same day of collection, samples were centrifuged and lipid profile was analyzed by methods described below in Biochemistry laboratory at Chengalpattu Hospital.

- Total Cholesterol: by cholesterol oxidase peroxidase method.
- Triglycerides: by glycerol phosphate oxidase peroxidase method.
- HDL: by direct detergent method.
- LDL: by Freidwalds calculation =TC-(HDL+TGL/5)
- All are enzymatic method.

As per NCEP ATPIII guidelines: LDL < 100mg/dl optimal, TC < 200 mg/dl desirable, HDL cholesterol < 40 low and ≥ 60 high, TGL< 150 mg/dl normal[67].

METHODOLOGY OF CARDIOVASCULAR AUTONOMIC FUNCTION TEST

Autonomic function was assessed using 4 noninvasive cardiovascular reflex tests. Each of the subjects was explained about the procedure and informed written consent was obtained. Cardiovascular reflex test were performed in the Research Lab of the Department of physiology, Chengalpattu Medical College, Chengalpattu between 8 am to 1pm in quiet room at temperature maintained between 25 to 28°C and the lighting subdued. Administration of any drugs or intravascular instrumentation was not involved in this test. Subjects were clearly instructed not to take any drugs, which may alter the autonomic functions and to avoid nicotine, coffee and cool drinks on the day of test. After 10 minutes of rest at lab to get accustomed to the new environment, history was taken and Clinical examinations were carried out to exclude out any acute or chronic illness and also for autonomic dysfunction. Resting pulse rate and blood pressure using manual sphygmomanometer were recorded.

METHODOLOGY OF HRV:

Subjects were clearly advised not to have coffee, tea or cool drinks at least 1½ hours prior to procedure. Before procedure individual was asked to

empty their bladder. Subject was instructed to lie down in supine position comfortable and relaxed.

PROCEDURE

After cleaning the skin surface with the spirit, in the following position ECG electrodes were fixed properly.

Exploring Electrode - Left shoulder/Forearm

Exploring Electrode - Right shoulder/Forearm

Reference Electrode - Right leg

The electrodes were connected to PHYSIOPAC equipment.

EQUIPMENT

Artifact free Lead II ECG was acquired using PHYSIOPAC PP8, MEDICATED SYSTEM,(INDIA) in such a way instantaneous heart rate at RR intervals were plotted using Kuopio's Finland version 2.2 software on a Microsoft Window based PC which helps to save multiple records, calculation tools, automated analysis and auto report generation. Short term HRV analysis was done after detrending using smoothness prior method with interpolation frequency of 4Hz.

i) Heart rate variability at supine rest

Lead II ECG was recorded for 20 minutes with eyes closed and with normal quiet respiratory movement (12-16/min).

ii) HR changes at one minute controlled deep breathing

Subjects were instructed to breathe slowly and **deeply inspiration for 5 seconds and expiration for 5 seconds at the rate of 6 breaths /minute,** who are under my command to do the deep breathing. Lead II ECG recording was continued throughout the procedure and the entire performance was monitored on the screen. Maximum Respiratory Sinus Arrhythmia will be produced by deep breathing. E/I ratio was calculated from **maximum RR intervals during expiration and minimum RR intervals during inspiration**[68].

iii) Heart Rate changes during Valsalva maneuver

Baseline Lead II ECG was recorded for 15 sec then subjects were asked to perform maneuver to exhale forcefully through the mouth piece of sphygmomanometer such that **Pressure was maintained in the manometer up to 40mmHg for 15 sec**. ECG recording continued during the maneuver and for about 30 sec after the maneuver. Valsalva ratio was calculated from maximum RR intervals during phase IV and minimum RR intervals during phase II [44, 69].

iv) Blood Pressure changes during Isometric Hand Grip Test

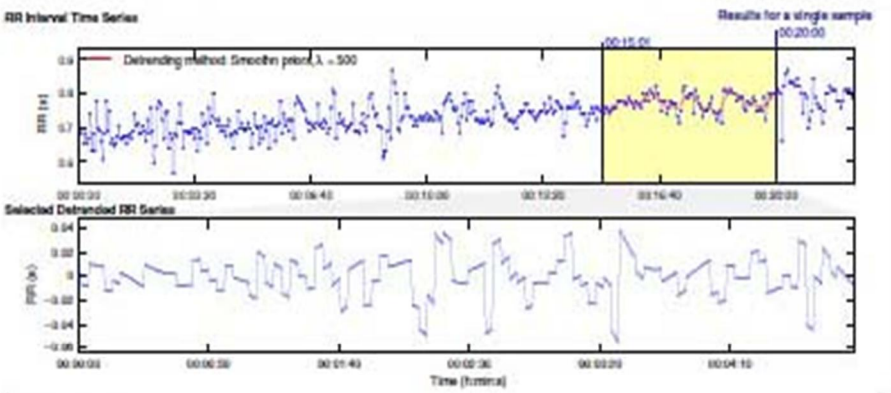
Resting blood pressure using manual sphygmomanometer was recorded in sitting position then subjects were asked to press the handle of dynamometer in dominant hand with maximum effort. The procedure was repeated thrice with rest in between and the best of the three was taken - as Maximum Voluntary Contraction (T max). After 5 minutes of rest, subjects were instructed to perform the same **isometric hand grip exercise in**

dominant hand at 30% of T max for 2 minutes, at the end of 2 minutes blood pressure was recorded on the other hand. Changes in systolic and diastolic blood pressure were noted. During procedure they were asked to breathe normally [70].

ETHICAL CONSIDERATIONS

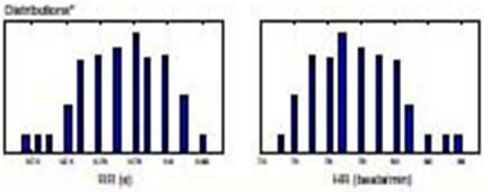
The study was approved by the Institutional Ethical Committee, Chengalpattu Medical College and Hospital, Chengalpattu.

HRV ANALYSIS REPORT



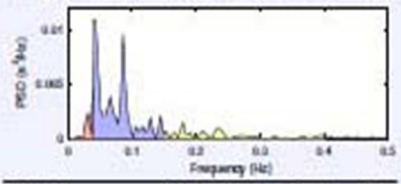
Time-Domain Results

Variable	Units	Value
Mean RR*	(ms)	773.1
STD RR (SDNN)	(ms)	16.4
Mean HR*	(1/min)	77.69
STD HR	(1/min)	2.22
RMSSD	(ms)	12.2
NN50	(count)	5
pNN50	(%)	1.3
RR triangular index		3.712
TINN	(ms)	75.0



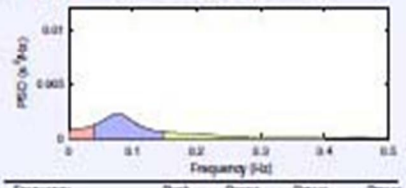
Frequency-Domain Results

FFT spectrum (Welch's periodogram: 256 s window with 50% overlap)



Frequency Band	Peak (Hz)	Power (ms²)	Power (%)	Power (n.u.)
VLF (0–0.04 Hz)	0.0391	33	9.2	
LF (0.04–0.15 Hz)	0.0400	267	74.7	82.2
HF (0.15–0.4 Hz)	0.1797	57	16.1	17.7
Total		356		
LF/HF		4.653		

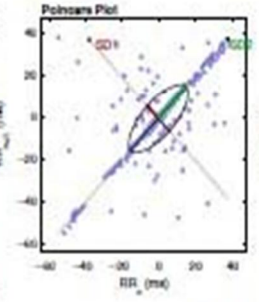
AR Spectrum (AR model order = 16, not factorized)

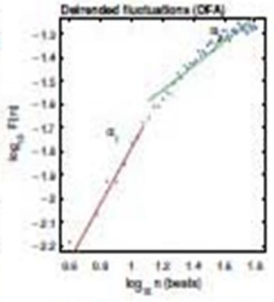


Frequency Band	Peak (Hz)	Power (ms²)	Power (%)	Power (n.u.)
VLF (0–0.04 Hz)	0.0391	37	15.0	
LF (0.04–0.15 Hz)	0.0781	159	64.5	75.9
HF (0.15–0.4 Hz)	0.1523	50	20.4	24.0
Total		245		
LF/HF		3.163		

Nonlinear Results

Variable	Units	Value
Poincare plot		
SD1	(ms)	8.6
SD2	(ms)	21.5
Recurrence plot		
Mean line length (Lmean)	(beats)	11.45
Max line length (Lmax)	(beats)	154
Recurrence rate (REC)	(%)	29.11
Determinism (DET)	(%)	99.15
Shannon Entropy (ShanEn)		3.206
Other		
Approximate entropy (ApEn)		0.840
Sample entropy (SampEn)		0.666
Detrended fluctuations (DFA) :α1		1.160
Detrended fluctuations (DFA) :α2		0.523
Correlation dimension (D2)		0.096
Multiscale entropy (MSE)		0.267 – 2.095





*Results are calculated from the non- detrended selected RR series

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Kubios HRV, 2.2
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OBSERVATION

TABLE 1: ANTHROPOMETRY OF SUBJECTS

PARAMETER	GROUP	N	MEAN±SD	STUDENT INDEPENDENT 't '-TEST
Age(in years)	CONTROL	30	32.37 ±2.86	t=1.449 p=0.153
	STUDY	30	33.4±2.66	
Height(in cm)	CONTROL	30	167.1±3.96	t= 1.303 p=0.198
	STUDY	30	165.43±5.79	
Weight(in kg)	CONTROL	30	62.5±5.16	t= 11.562 **p<0.001****
	STUDY	30	79.87±6.42	
BMI(kg/m^2)	CONTROL	30	21.73±1.64	t= 16.658 **p<0.001****
	STUDY	30	28.7±1.60	
WC (in cm)	CONTROL	30	77.77±4.52	t= 12.353 **p<0.001****
	STUDY	30	89.5±2.57	
HC (in cm)	CONTROL	30	88.17±4.1	t= 9.013 **p<0.001****
	STUDY	30	96.3±2.77	
WHR	CONTROL	30	0.88±0.02	t= 8.19 **p<0.001****
	STUDY	30	0.93±0.02	

Anthropometric measurements are expressed as mean ± SD

*p<0.05 is significant, **p<0.01 is highly significant

TABLE 2: COMPARISON OF RESTING HEART RATE AND BLOOD PRESSURE BETWEEN TWO GROUPS.

PARAMETERS	CONTROL (N=30)	STUDY (N=30)	STUDENT INDEPENDENT t - TEST	
	MEAN±SD	MEAN±SD		
Mean HR(bpm)	71.38±5.35	75.09±8.00	t= 2.113	**p=0.039***
SBP (mmHg)	112.73±8.23	120.53±4.30	t= 4.602	**p<0.001****
DBP (mmHg)	71.73±7.06	76.07±4.09	t= 2.91	**p=0.005****
PP (mmHg)	41±5.84	44.47±3.13	t= 2.863	**p=0.006****
MAP(mmHg)	85.4±6.94	90.89±3.89	t=3.778	**P<0.001****

Data are expressed as mean ± SD, 95% confidence interval of the mean.

*p<0.05 is significant, **p<0.01 is highly significant.

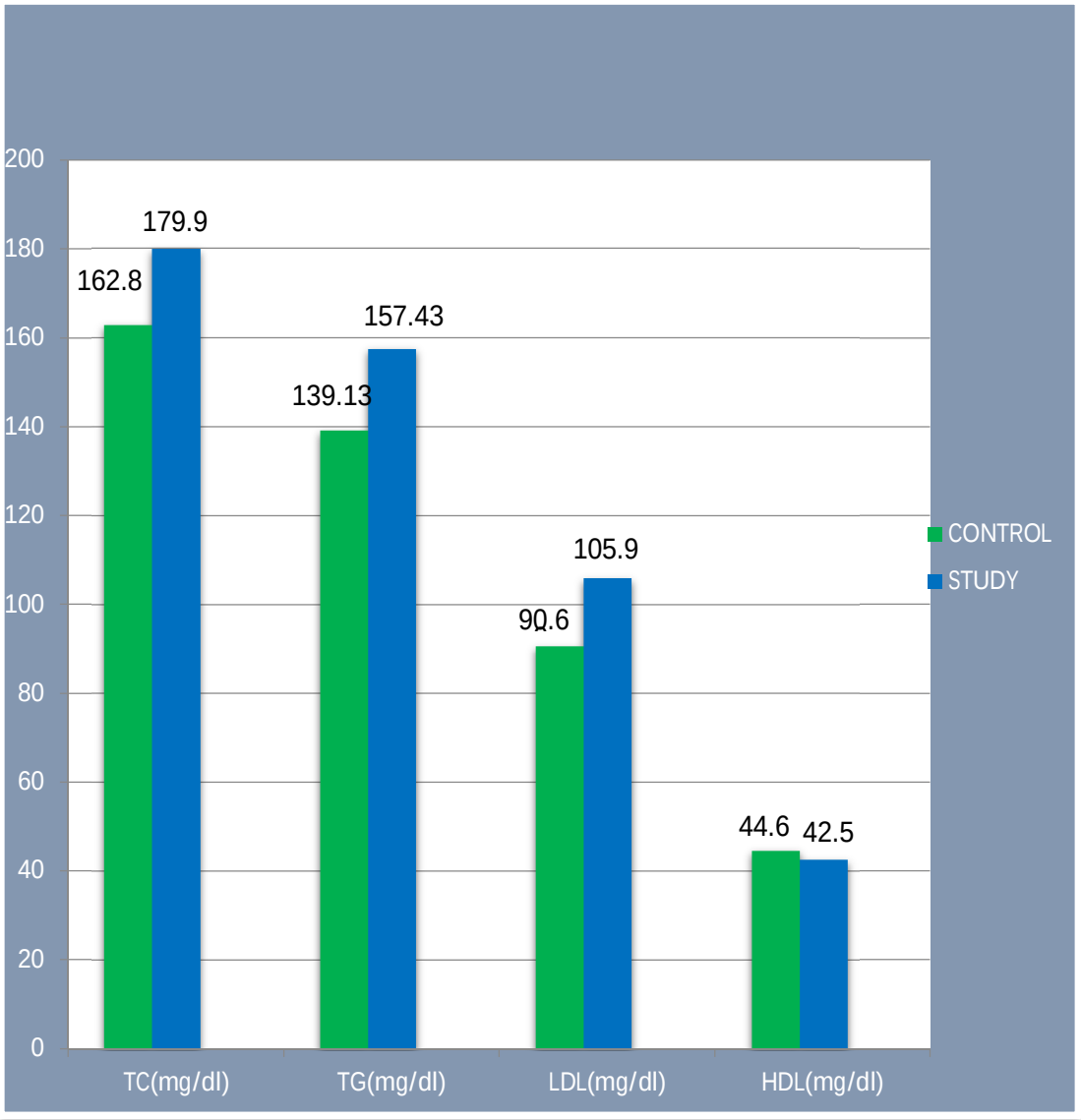
TABLE 3: COMPARISON OF LIPID PROFILE PARAMETERS BETWEEN TWO GROUPS.

PARAMETERS	CONTROL (N=30)	STUDY (N=30)	STUDENT INDEPENDENT t-TEST
	MEAN±SD	MEAN±SD	
TC (mg/dl)	162.83±10.18	179.93±10.42	t= 6.431 **p=0.001****
TGL (mg/dl)	139.13±13.15	157.43±10.40	t= 5.979 **p=0.001****
LDL (mg/dl)	90.67±7.54	105.97±8.7	t= 7.279 **p=0.001****
HDL (mg/dl)	44.63±2.63	42.57±1.74	t= 3.59 **p=0.001****

Data are expressed as mean ± SD, 95% confidence interval of the mean.

*p<0.01 is highly significant.

FIGURE: 4 COMPARISON OF LIPID PROFILE PARAMETERS BETWEEN CONTROL GROUP AND STUDY GROUP



This figure shows increase TC, TGL and LDL and decrease HDL in study group compared to control group

TABLE4: COMPARISON OF HRV INDICES TIME DOMAIN MEASURES BETWEEN TWO GROUPS DURING SUPINE REST.

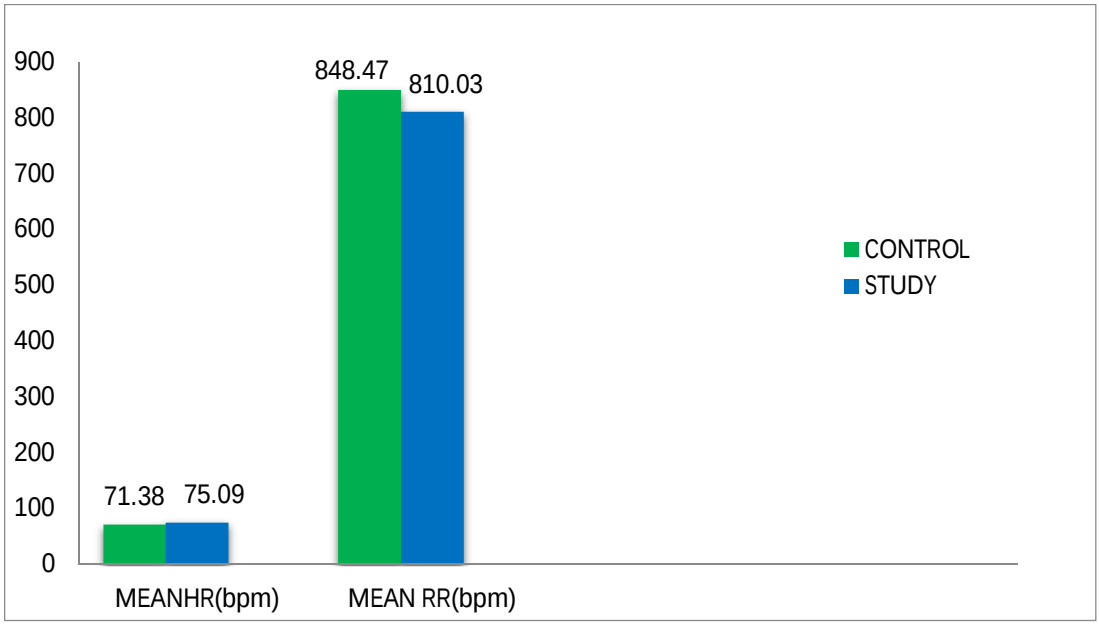
TIME DOMAIN MEASURES	CONTROL (N=30)	STUDY (N=30)	STUDENT INDEPENDENT t –TEST	
	MEAN±SD	MEAN±SD	t value	P value
MEAN RR (ms)	848.47±59.62	810.03±85.76	2.015	**0.04***
MEAN HR (bpm)	71.38±5.35	75.09±8.00	2.113	**0.039***
SDNN(ms)	33.39±12.99	23.17±9.37	3.496	**0.001****
RMSSD (ms)	26.26±10.65	17.37±7.996	3.656	**0.001****
NN50 COUNT	22.03±13.8	11.05±9.85	3.404	**0.001****
pNN50 (%)	6.2±3.81	3.19±2.81	3.473	**0.001****

Data are expressed as mean ± SD, 95% confidence interval of the mean.

*$p<0.05$ significant,

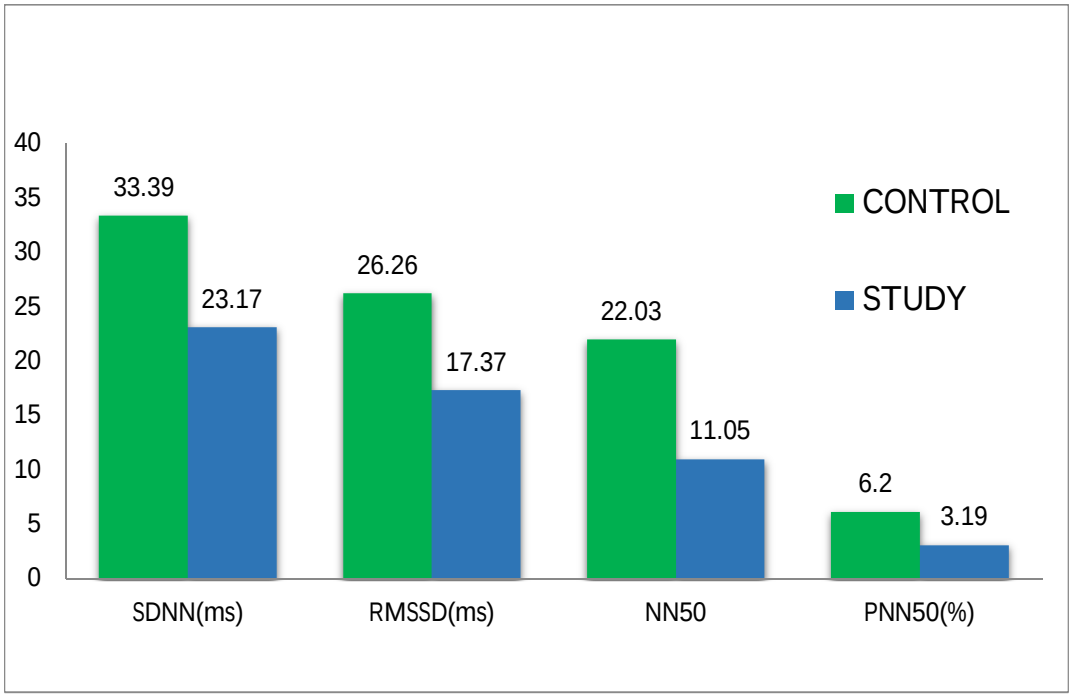
**$p<0.01$ highly significant.

FIGURE: 5 COMPARISON OF MEAN HR AND MEAN RR BETWEEN CONTROL AND STUDY GROUP AT SUPINE REST



This figure shows increase Mean HR and decrease Mean RR in study group compared to control group

FIGURE: 6 COMPARISON OF TIME DOMAIN MEASURES BETWEEN CONTROL AND STUDY GROUP AT SUPINE REST



This figure shows decrease in SDNN, RMSDD, NN50, pNN50% in study group compared to control group.

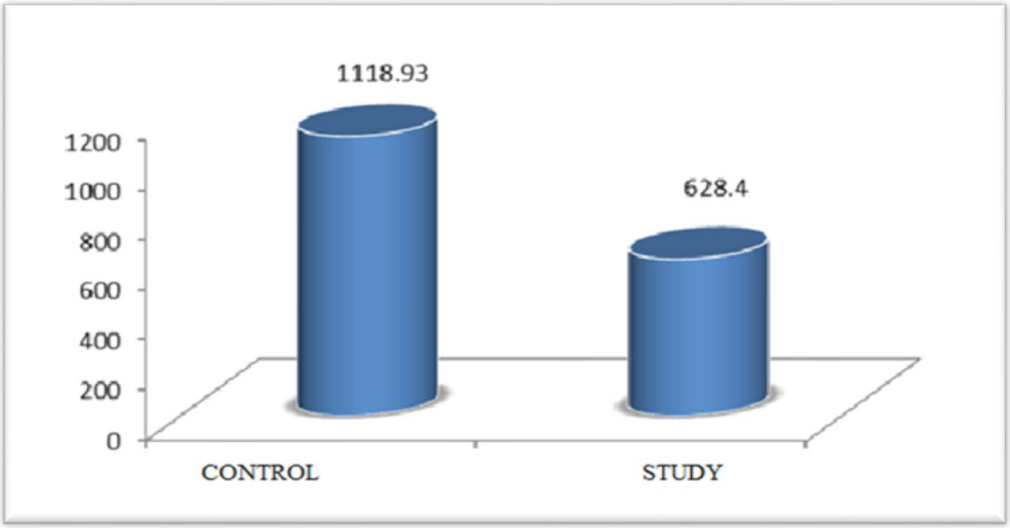
TABLE 5: COMPARISON OF HRV INDICES FREQUENCY DOMAIN MEASURES BETWEEN TWO GROUPS DURING SUPINE REST.

FREQUENCY DOMAIN MEASURES	CONTROL (N=30)	STUDY (N=30)	STUDENT INDEPENDENT t - TEST	
	MEAN±SD	MEAN±SD	t value	P value
MEAN RR (ms)	848.46±59.62	810.03±85.76	t= 2.015	**p=0.04***
TOTAL POWER ms^2	1118.93±763.07	628.4±780.26	t= 2.462	**p=0.017***
LF n.u.	73.59±4.16	80.52±3.53	t= 6.96	**P<0.001****
HF n.u.	26.24±4.26	19.39±3.54	t= 6.766	**P<0.001****
LF/HF RATIO	2.89 ±0.54	4.32±0.97	t=7.045	**P<0.001***

Data are expressed as mean ± SD, 95% confidence interval of mean

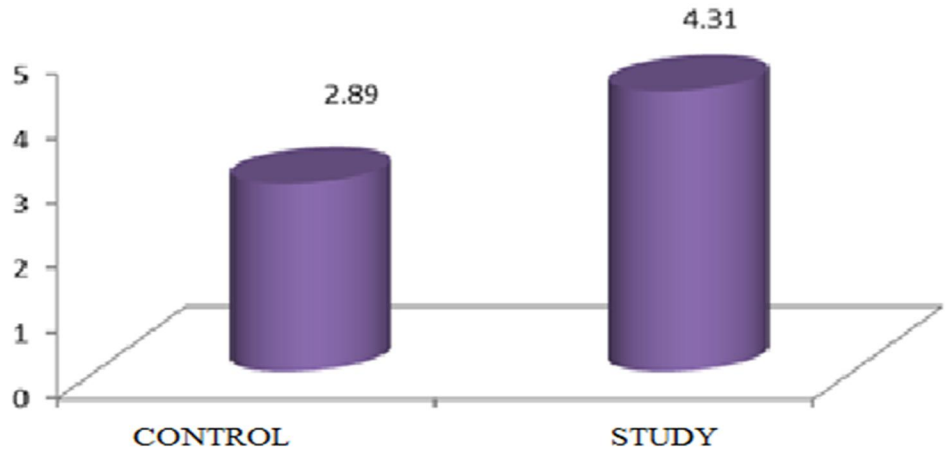
*p< 0.05 significant, **p< 0.01 highly significant.

FIGURE: 7 COMPARISON OF TOTAL POWER (ms^2) BETWEEN CONTROL GROUP AND STUDY GROUP AT SUPINE REST



This figure shows decrease Total power in study group compared to control group

FIGURE: 8 COMPARISON OF LF / HF RATIO BETWEEN CONTROL GROUP AND STUDY GROUP AT SUPINE REST



This figure shows increase LF/HF ratio in study group compared to control group.

TABLE 6: COMPARISON OF HRV INDICES AND E/I RATIO BETWEEN TWO GROUPS DURING ONE MINUTE CONTROLLED DEEP BREATHING.

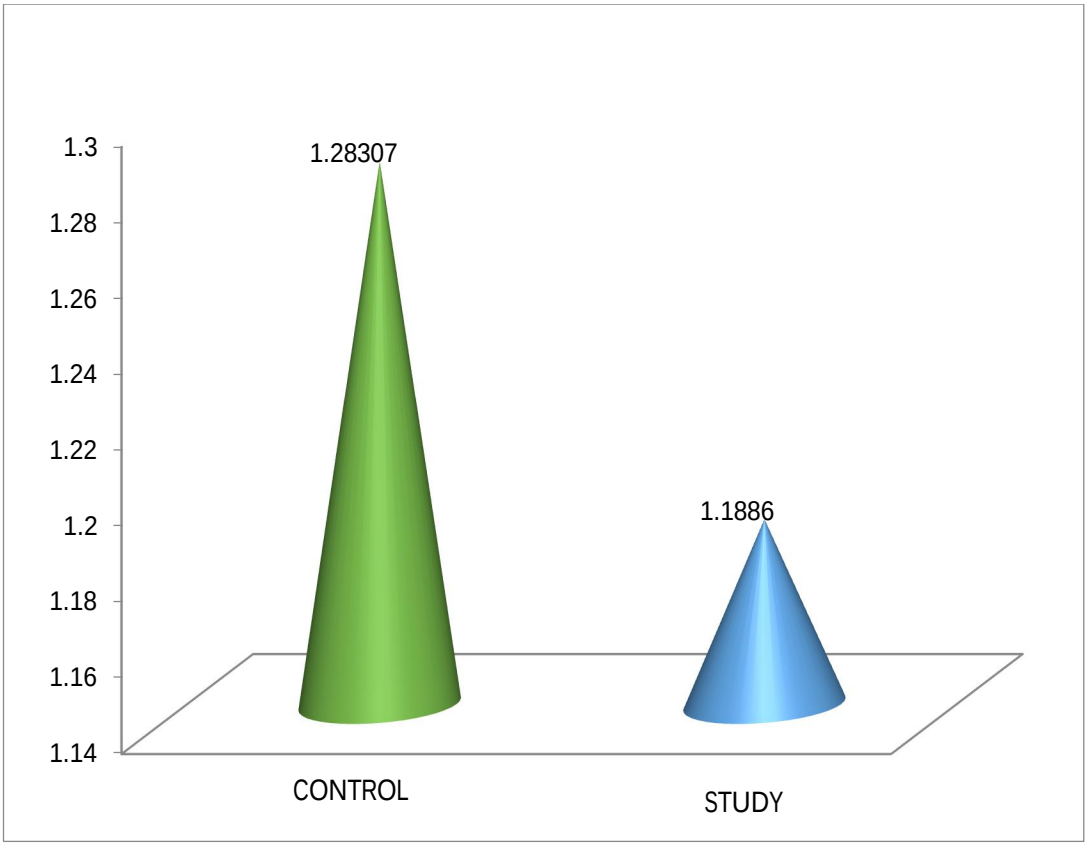
HRV INDICES AND E/I RATIO	CONTROL (N=30)	STUDY (N=30)	STUDENT INDEPENDENT t-TEST	
	MEAN±SD	MEAN±SD	t value	P value
MEAN HR (bpm)	75.54±7.28	75.26±8.76	0.134	0.893
MEAN RR (ms)	817.76±82.87	816.18±98.44	0.067	0.947
SDNN (ms)	98.48±30.16	69.56±36.28	3.358	**0.001****
HF n.u.	35.83±10.65	30.66±7.47	2.178	**0.034***
E/I	1.28±0.10	1.19±0.11	3.4	**0.001****

Data are expressed as mean ± SD, 95% confidence interval of the mean.

*$p<0.05$ significant,

**$p< 0.01$ highly significant.

FIGURE: 9 COMPARISON OF E/I RATIO BETWEEN CONTROL GROUP AND STUDY GROUP



This figure shows decrease E/I ratio in study group compared to control group.

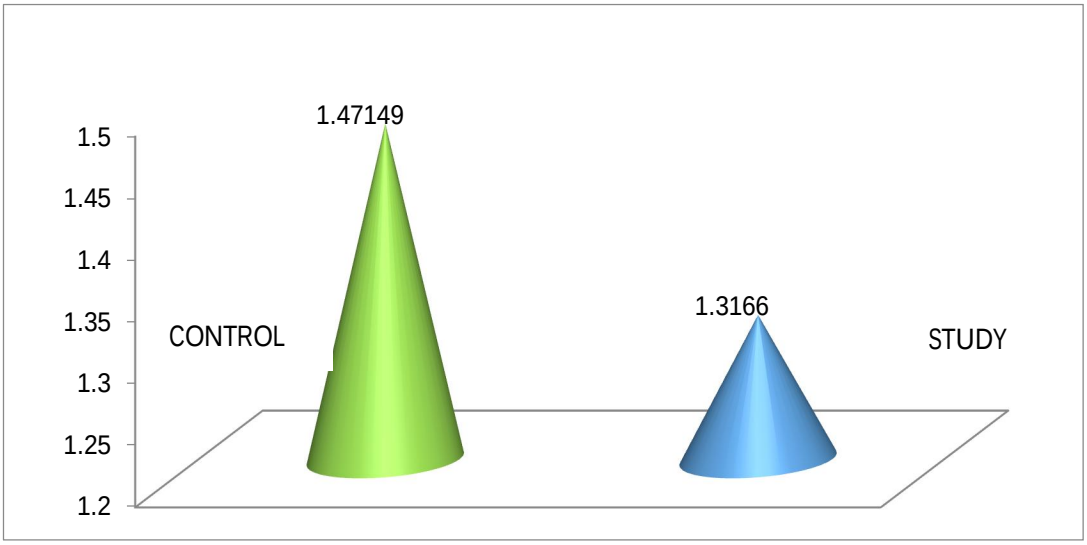
TABLE 7: COMPARISON OF VALSALVA RATIO BETWEEN TWO GROUPS

VALSALVA RATIO	CONTROL (N=30)	STUDY (N=30)	STUDENT INDEPENDENT t- TEST
	MEAN±SD	MEAN±SD	
MAXRR/MIN RR (ms)	1.47±0.27	1.32±0.22	t= 2.429 **p=0.018***

Data are expressed as mean ± SD, 95% confidence interval of the mean.

*p< 0.05 significant,

FIGURE: 10 COMPARISON OF VALSALVA RATIO BETWEEN CONTROL GROUP AND STUDY GROUP



This figure shows decrease Valsalva ratio in study group compared to control group

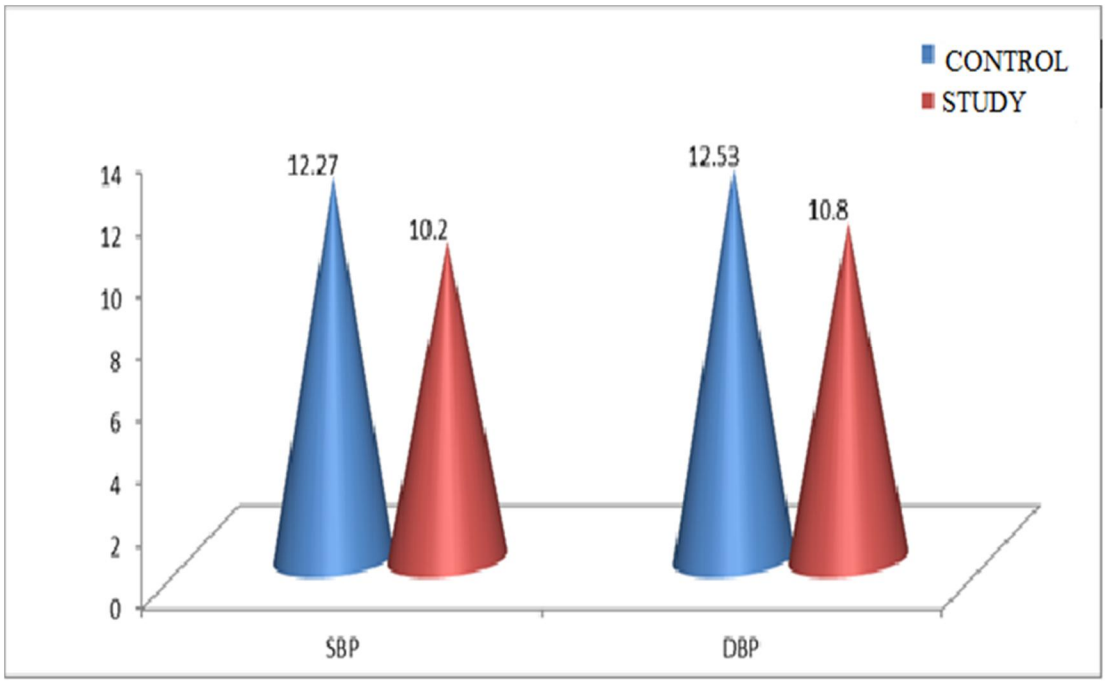
TABLE 8: COMPARISON OF ISOMETRIC HAND GRIP BETWEEN TWO GROUPS

PARAMETERS	CONTROL (N=30)	STUDY (N=30)	STUDENT INDEPENDENT t- TEST
	MEAN±SD	MEAN±SD	
Systolic blood pressure difference (mmHg)	12.27±4.03	10.2±2.75	t= 2.323 **p=0.024***
Diastolic blood pressure difference (mmHg)	12.53±2.87	10.8±2.76	t= 2.383 **p=0.02***

Data are expressed as mean ± SD, 95% confidence interval of the mean.

*p<0.05 significant

FIGURE: 11 COMPARISON OF ISOMETRIC HANDGRIP BETWEEN CONTROL GROUP AND STUDY GROUP



This figure shows rise of SBP and DBP in study group is less compared to control group.

TABLE 9: CORRELATION BETWEEN BMI, WC, AND WHR AND SDNN, TP AND LF/HF RATIO.

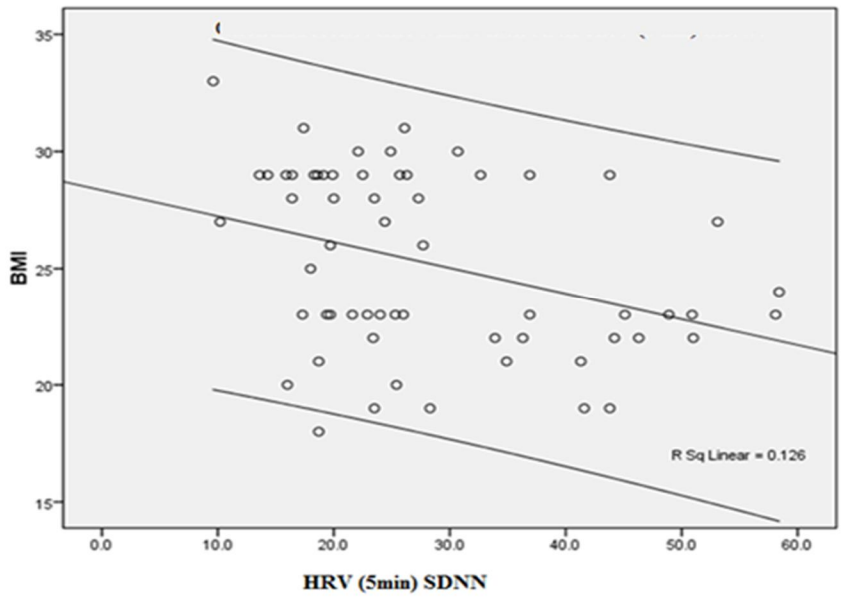
N=60	BMI(Kg/m^2)	WC(cm)	WHR
SDNN(ms)	-0.336 **0.009****	-0.303 **0.018***	-0.246 0.058
TOTAL POWER(ms^2)	-0.405 **0.001****	-0.347 **0.007****	-0.291 **0.024***
LF/HF RATIO	0.603 **0.001****	0.618 **0.001****	0.51 **0.001****

Data are expressed as spearman correlation coefficient r, and P value respectively, 95% confidence interval of R are mentioned when P values are ~ 0.05.

*p< 0.05 significant,

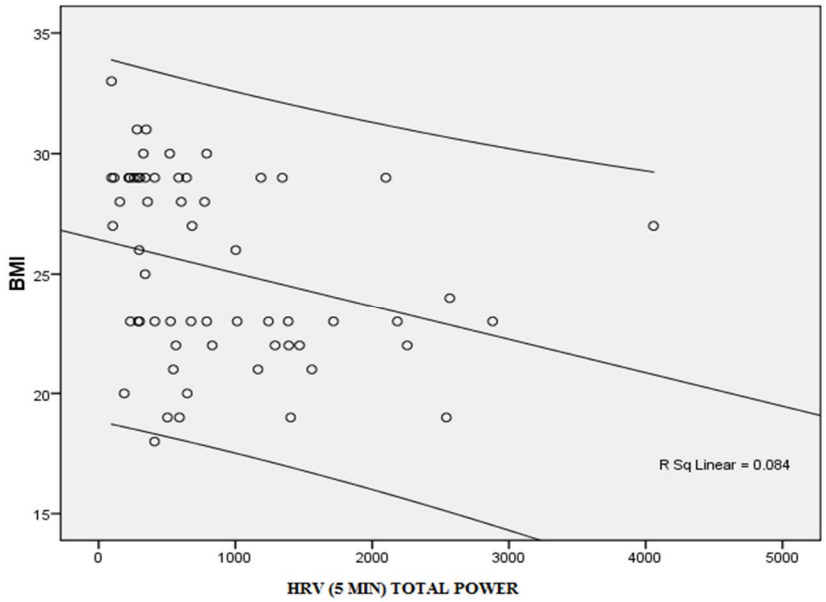
** p<0.01 highly significant.

FIGURE: 12 CORRELATION BETWEEN BMI AND HRV (5 min) SDNN



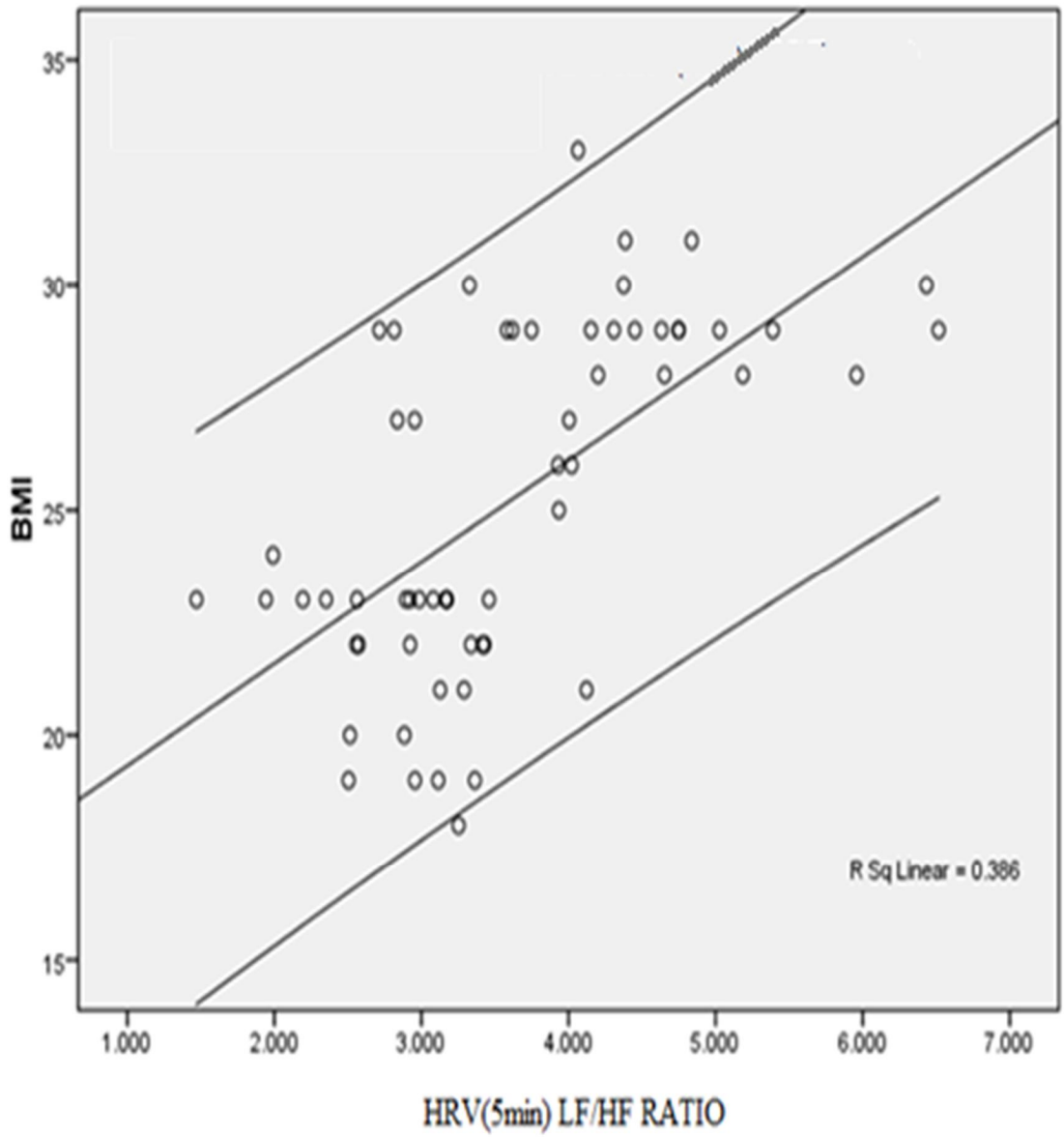
This figure shows negative correlation between BMI and SDNN.

FIGURE: 13 CORRELATION BETWEEN BMI AND HRV(5 min) TOTAL POWER



This figure shows negative correlation between BMI and Total power.

FIGURE: 14 CORRELATION BETWEEN BMI AND HRV(5MIN) LF/HF RATIO



This figure shows positive correlation between BMI and LF/HF RATIO.

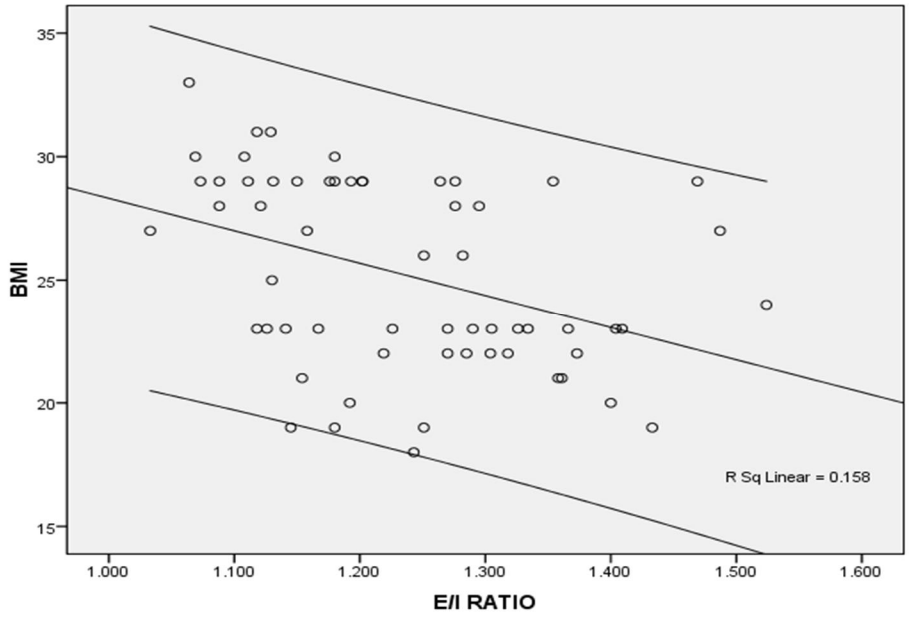
TABLE 10: CORRELATION BETWEEN BMI, WC AND WHR AND E/I RATIO AND VALSALVA RATIO.

N=60	BMI(Kg/m2)	WC(cm)	WHR
E/I RATIO	-0.44 **0.001****	-0.433 **0.001****	-0.424 **0.001****
VALSALVA RATIO	-0.344 **0.007****	-0.254 0.05	-0.22 0.091

*p< 0.05 significant

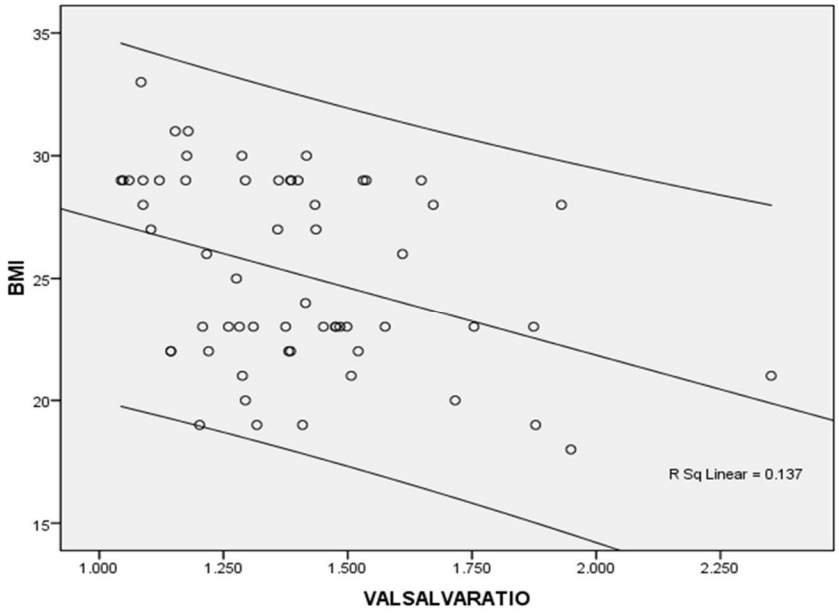
** p<0.01 highly significant.

FIGURE: 15 CORRELATION BETWEEN BMI AND E/IRATIO



This figure shows negative correlation between BMI and E/I RATIO

FIGURE: 16 CORRELATION BETWEEN BMI AND VALSALVA RATIO



This figure shows negative correlation between BMI and Valsalva ratio.

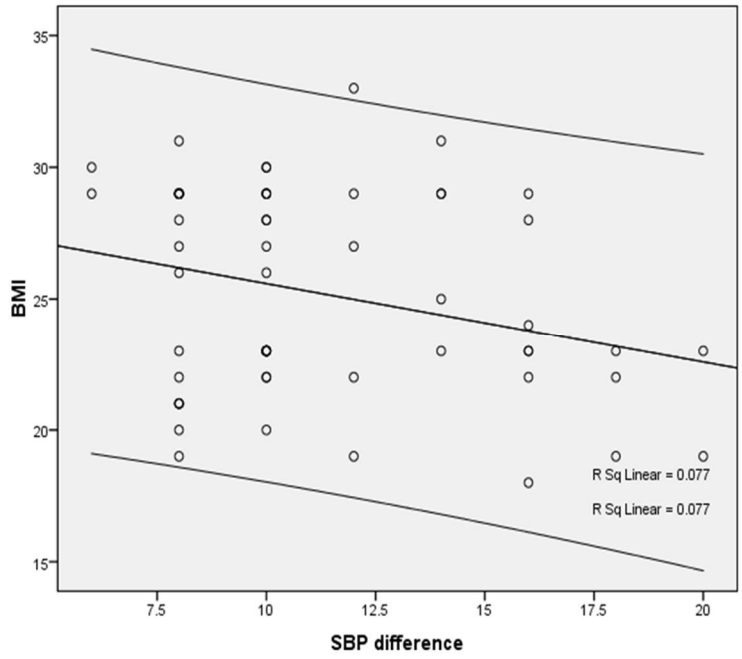
TABLE 11: CORRELATION BETWEEN BMI, WC AND WHR AND ISOMETRIC HAND GRIP

N=60		BMI(Kg/m2)	WC(cm)	WHR
IHG	SBP difference(mmHg)	-0.207 0.112	-0.166 0.204	-0.212 0.104
	DBP Difference (mmHg)	-0.262 **0.043***	-0.225 0.084	-0.18 0.17

Data are expressed as spearman correlation coefficient r, and P value respectively, 95% confidence interval of R are mentioned when P values are~ 0.05.

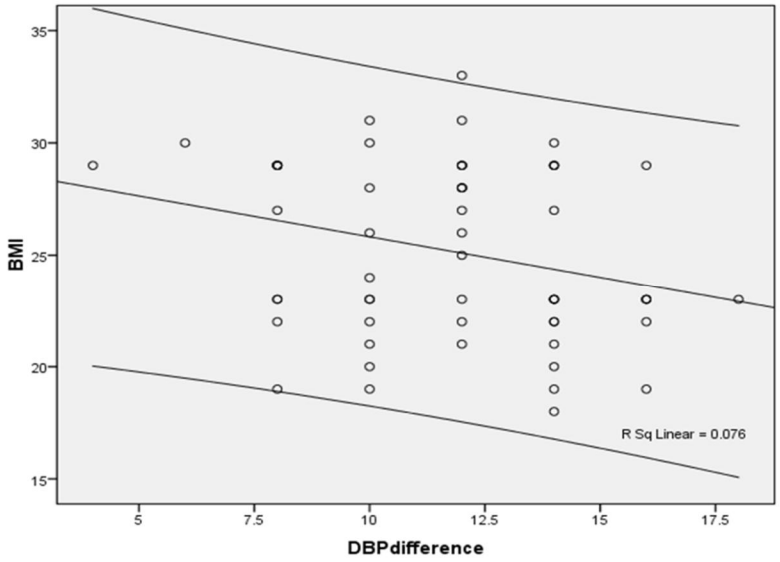
*p< 0.05 significant.

FIGURE: 17 CORRELATION BETWEEN BMI AND SYSTOLIC BLOOD PRESSURE DIFFERENCE



This figure shows negative correlation between BMI and SBP difference during IHGT

FIGURE: 18 CORRELATION BETWEEN BMI AND DIASTOLIC BLOOD PRESSURE DIFFERENCE



This figure shows negative correlation between BMI and DBP difference during IHGT.

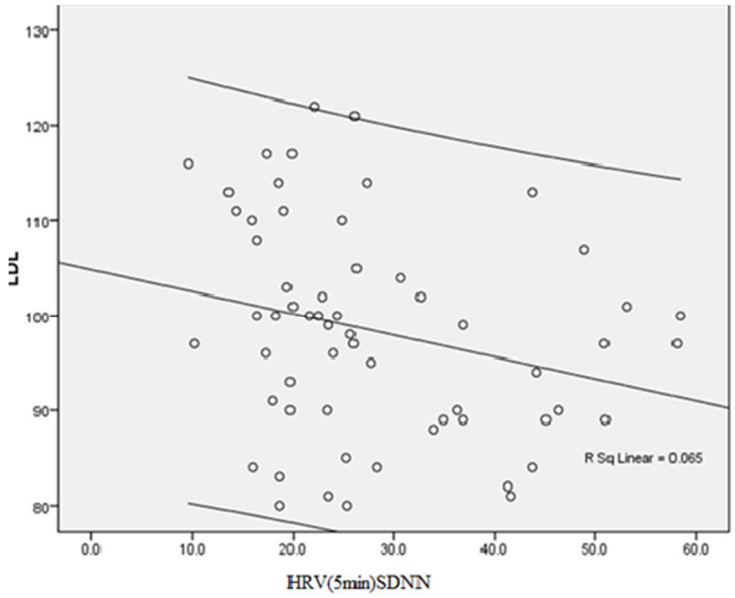
TABLE12: CORRELATION BETWEEN LIPID PROFILE AND SDNN, TOTAL POWER AND LF/HF RATIO.

N=60	**TC (mg/dl)**	**TGL (mg/dl)**	**LDL (mg/dl)**	**HDL (mg/dl)**
SDNN (ms)	-0.26 **0.045***	-0.213 0.102	-0.285 **0.027***	0.142 0.278
TOTAL POWER (ms^2)	-0.284 **0.028***	-0.25 0.054	-0.322 **0.012***	0.203 0.121
LF/HF RATIO	0.53 **0.001****	0.488 **0.001****	0.582 **0.001****	-0.309 **0.016***

Data are expressed as spearman correlation coefficient r, and P value respectively, 95% confidence interval of R are mentioned when P values are~ 0.05.

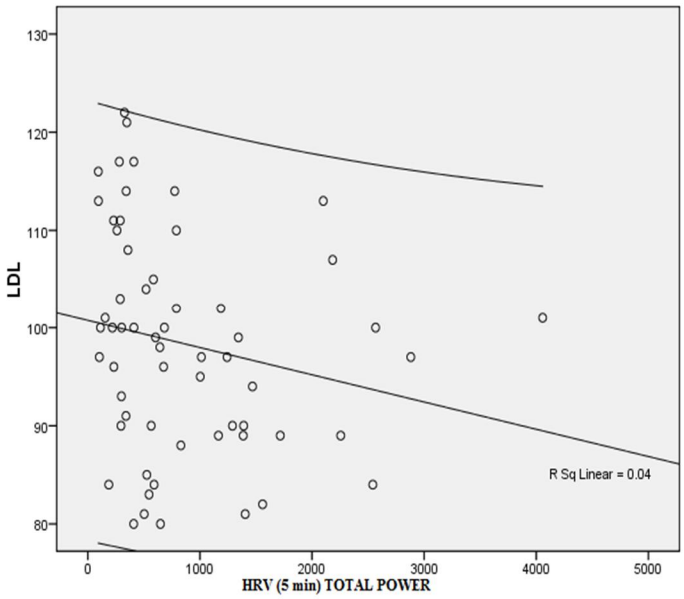
*p< 0.05 significant, **p<0.01 highly significant.

FIGURE: 19 CORRELATION BETWEEN LDL AND HRV (5 min) SDNN



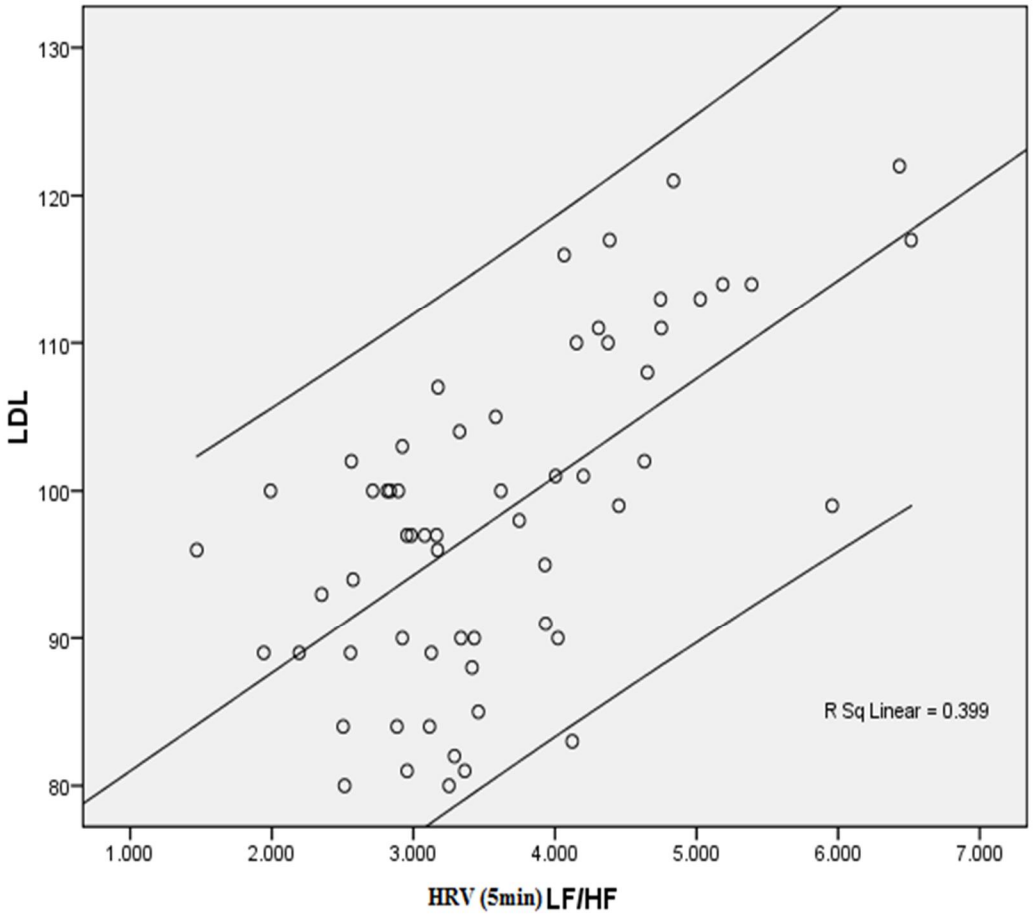
This figure negative shows negative correlation between LDL and SDNN.

FIGURE: 20 CORRELATION BETWEEN LDL AND HRV(5 min) TOTALPOWER



This figure negative shows negative correlation between LDL and Total power

FIGURE: 21 CORRELATION BETWEEN LDL AND HRV (5 min) LF/HF RATIO



This figure negative shows positive correlation between LDL and LF/HF ratio.

TABLE 13: CORRELATION BETWEEN LIPID PROFILE AND E/I RATIO AND VALSALVA RATIO.

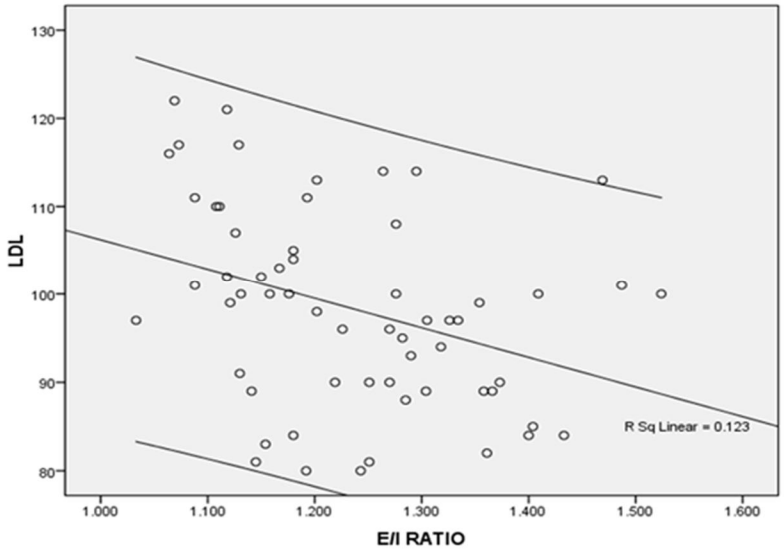
.N=60	TC (mg/dl)	TGL (mg/dl)	LDL (mg/dl)	HDL (mg/dl)
E/I RATIO	-0.376 **0.003****	-0.367 **0.004****	-0.405 **0.001****	0.2 0.125
VALSALVARATIO	-0.297 **0.021***	-0.252 0.052	-0.27 **0.037***	0.067 0.61

Data are expressed as spearman correlation coefficient r, and P value respectively, 95% confidence interval of R are mentioned when P values are~ 0.05.

*p< 0.05 significant

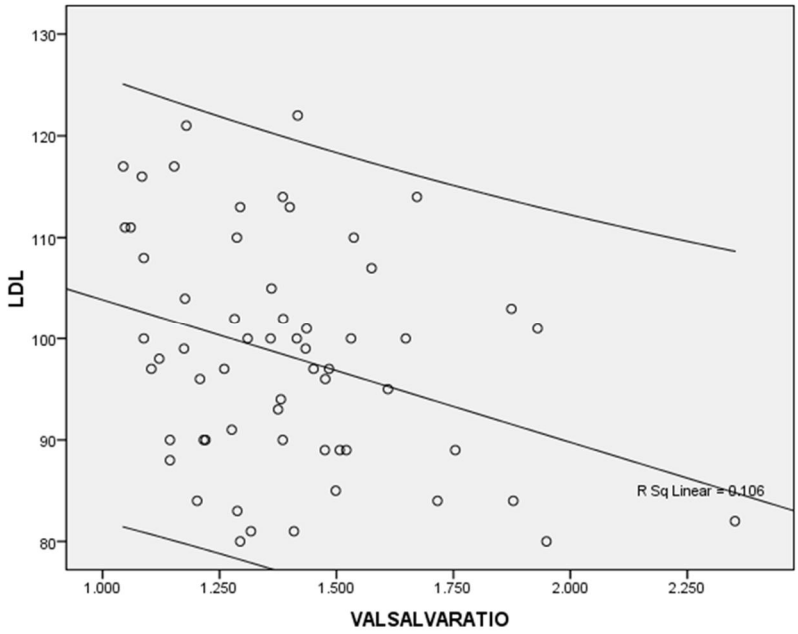
**p<0.01 highly significant.

FIGURE: 22 CORRELATION BETWEEN LDL AND E/I RATIO



This figure shows negative correlation between LDL and E/ I RATIO.

FIGURE: 23 CORRELATION BETWEEN LDL AND VALSALVA RATIO



This figure shows negative correlation between LDL and Valsalva ratio.

TABLE 14: CORRELATION BETWEEN LIPID PROFILE AND ISOMETRIC HAND GRIP.

N=60		**TC(mg/dl)**	**TG(mg/dl)**	**LDL(mg/dl)**	**HDL(mg/dl)**
IHG	SBP Difference (mmHg)	-0.167 0.201	-0.097 0.459	-0.165 0.209	0.017 0.9
	DBP difference (mmHg)	-0.282 **0.029***	-0.162 0.216	-0.251 0.053	0.006 0.963

Data are expressed as spearman correlation coefficient r, and P value respectively, 95% confidence interval of R are mentioned when P values are~ 0.05.

*p<0.05significant

RESULTS

Statistical Package for Social Sciences (SPSS) 16 version was used for Statistical analysis. The present study includes 60 subjects (30 0bese and 30 non-obese)

Table 1-8 were analyzed using student independent unpaired ‘t’ test

Table 1: Anthropometric characteristic of subjects are expressed as mean ± SD

Shows significant difference in weight, BMI, waist circumference, hip circumference and waist hip ratio between control group and study group, (**p<0.01) no significant difference in age and height.

Table 2: Comparison of Resting Heart Rate and Blood Pressure expressed as mean± SD

Shows significant difference in HR (* p<0.05), SBP, DBP, PP and MAP between control group and study group (**p<0.01).

Table 3: Comparison of Lipid profile parameters expressed as mean ± SD

Shows significant increase in TC, TGL and LDL in study group as compared to control group (**p<0.01). Also shows, significant decrease in HDL in study group as compared to control group (**p<0.01).

Table 4: Comparison of HRV indices time domain measures at supine rest expressed as mean ± SD

Shows significant increase in HR and decrease in RR interval in study group as compared to control group (*p<0.05). Also shows, significant decrease in SDNN, RMSSD, NN50 and PNN50% in study group as compared to control group indicating decreased parasympathetic activity (**p<0.01).

Table 5: Comparison of HRV indices frequency domain measures at supine rest expressed as mean ± SD

Shows significant increase in LF nu, LF/HF ratio in study group as compared to control group (**p<0.01). Also shows significant decrease in Total power (* p<0.05) and HF nu (**p<0.01) in study group as compared to control group.

Table 6: Comparison of HRV indices and E/I at one minute controlled deep breathing expressed as mean ±SD

Shows no significant difference in Mean HR and Mean RR between study group and control group. Also shows, significant decrease in SDNN (**p<0.01), HF nu (*p<0.05) and E/I ratio (**p<0.01) in study group as compared to control group

Table 7: Comparison of Valsalva ratio between control and study group expressed as mean± SD.

Shows significant decrease in Valsalva ratio in study group as compared to control group (*p<0.05).

Table 8: Comparison of Isometric hand grip between control and study groups expressed as mean ±SD.

Shows significant decrease in rise of SBP and DBP in study group as compared to control group (* $p<0.05$).

The cardiovascular autonomic function test was correlated with anthropometric indices and lipid profile parameters by spearman correlation coefficient.

Table 9: Correlation between Anthropometric parameters and SDNN, TP and LF/HF ratio of Resting HRV.

BMI shows significant negative correlation with SDNN, TP and LF/ HF ratio (**$p<0.01$). WC also shows negative correlation with SDNN, TP and LF/HF ratio significantly (*$p<0.05$). WHR shows negative correlation with TP and LF/HF ratio significantly (*$p<0.05$) and with SDNN insignificantly.

Table 10: Correlation between Anthropometric parameters and E/I ratio and Valsalva ratio

BMI shows significant negative correlation with E/I ratio and Valsalva ratio (**$p<0.01$). WC shows negative correlation with E/I ratio significantly (**$p<0.01$) and Valsalva ratio insignificantly. WHR also shows negative correlation with E/I ratio significantly (**$p<0.01$) and Valsalva ratio insignificantly.

Table 11: Correlation between Anthropometric parameters and Isometric hand grip test

BMI shows negative correlation with rise of DBP significantly (*p<0.05) and SBP insignificantly. WC and WHR also show negative correlation with rise of SBP and DBP insignificantly.

Table 12: Correlation between Lipid profile and SDNN, TP and LF/HF ratio of Resting HRV.

TC, LDL shows significant negative correlation with SDNN, TP (*p<0.05) and positive correlation with LF/HF ratio (**p<0.01). TGL shows negative correlation with SDNN, TP insignificantly and positive correlation with LF/HF significantly (**p<0.01). HDL shows positive correlation with SDNN and TP though insignificant and negative correlation with LF/HF ratio significantly (*p<0.05).

Table 13: Correlation between Lipid profile and E/I ratio and Valsalva ratio

TC and LDL shows significant negative correlation with E/I ratio (**p<0.01) and Valsalva ratio (*p<0.05). TGL shows negative correlation with E/I ratio significantly (**p<0.01) and Valsalva ratio insignificantly. HDL positively correlated with E/I ratio and Valsalva ratio though not significant.

Table14: Correlation between Lipid profile and Isometric hand grip test .

TC, TGL and LDL were negatively correlated with rise of SBP but not significant.TC shows negative correlation with rise of DBP significantly (*$p<0.05$). TGL and LDL also shows negative correlation with rise of DBP but not significant. HDL shows positive correlation with rise of SBP and DBP but not significant.

DISCUSSION

Obesity is one of the common health problems in the community. Obesity and its related comorbidities like metabolic and cardiovascular diseases increases day by day. Though it reduces life expectancy of individuals, it is one of the preventable risks. In Obesity, the commonly altered metabolism is lipid. This abnormal lipid profile increases the risk of atherosclerosis and adverse cardiovascular events. Autonomic nervous system influences cardiovascular system under resting conditions. The heart rate and blood pressure is regulated by the ANS which in turn is influenced by arterial baroreflex mechanism. Thereby arterial baroreflex mechanism also plays a role in cardiovascular regulation. Obesity and abnormal lipid profile impairs autonomic and baroreceptor regulation of cardiovascular system and predisposes to certain cardiovascular disease.

Hence the present study was to evaluate lipid profile and autonomic function test of obese male individuals using cardiovascular autonomic function test and to correlate anthropometric parameters and lipid profile with autonomic function test. According to EWING'S CRITERA, abnormal response in two or more of the heart rate test indicates definite Autonomic involvement[43, 60]**.** Cardiovascular autonomic reflex tests including Heart Rate Variability, Deep Breathing, Valsalva Maneuver and Isometric Hand Grip were carried out to quantify autonomic dysfunction. The test that asses parasympathetic function are time domain measures and high frequency

component of resting HRV, E/I ratio of deep breathing and Valsalva ratio. The test that asses sympathetic function are low frequency component of resting HRV and Isometric hand grip test.

CHARACTERISTIC OF STUDY SUBJECTS

Obese male individuals of BMI >25kg/m^2 were enrolled as study group and normal individuals of BMI< 22.9 kg/m^2 were enrolled as control group. The mean age of obese and non – obese individuals included in this study were 33.4±2.66 and 32.37±2.86, there was no significant differences. This shows change in autonomic nervous system activity is due to excess body fat rather than age.

The body mass index was calculated by the formula, weight in (kg) / Height in (m^2) and Waist Hip Ratio by the formula, waist circumference/ Hip circumference. The mean BMI of study group and control group shows statistically significant difference (*$p<0.01$). The mean WC and WHR of study group and control group also shows statistically significant differences (*$p<0.01$). (Table 1) This shows altered lipid profile and autonomic activity is due to excess body fat.

According to Deepan Stephen et al[49], the prevalence of generalized and abdominal obesity increases until the age of 50 in both the gender and both associated with cardio metabolic risk. According to Hirsh et al[71], when body weight increases by 10%, there was reduced parasympathetic activity.

RESTING HEART RATE AND BLOOD PRESSURE

In this study, the mean RHR was higher in study group (75.09±8.00) compared to control group (71.38±5.35), significantly with (*p<0.05). According to Ravikeerthy et al[72], (2015) Kanavi roopa shekarappa et al[2], (2011) and Ajay et al[73], (2014) resting heart rate was higher in obese group. Increased resting heart rate in obesity is due to reduced parasympathetic activity and increased sympathetic activity.

The mean SBP and DBP in study group were (120.53±4.30 and 76.07±4.09) and in control group were (112.73±8.23 and 71.73±7.06) respectively. The mean PP and MAP in study group were (44.47 ±3.13 and 90.89±3.89) and in control group were (41±5.84 and 85.4±6.94) respectively. The resting SBP, DBP, PP and MAP were significantly increased in the study group as compared to control group with (**p< 0.01). (Table2)

This is similar to findings observed in other studies conducted in different age group. According to Kanavi roopa shekarappa et al[2], (2011) study, SBP, DBP, PP and MAP were significantly higher in study group compared to control group of age 21 to 60 years. However based on age distribution, they found DBP was not significant in obese in the age group of 31 to 40 years. Ravikeerthy et al[72], (2015) revealed that SBP, DBP, PP and MAP were significantly higher in obese group compared to non-obese group. Ajay et al[73], (2014) also demonstrated higher BP in obese group but in younger age (15-19years).

The higher resting SBP, DBP in obese individuals is due to increase vasoconstrictor tone and increase in blood volume and cardiac output as a result of increased metabolic demand. The metabolic demand increases as additional blood flow is required for extra adipose tissue. The increase in peripheral resistance is due to sympathetic over activity, endothelial dysfunction, insulin resistance and cytokines from adipose tissue. Other mechanisms involved in sympathetic activation and high BP may be hyperleptinemia, hyperinsulinemia, free fatty acids and Renin angiotensin-aldosterone activation. (Srinath et al, 2011)[74]. In obesity, there is a rise of heart rate and blood pressure even under resting conditions which contributes to CV dysfunction at an earlier stage.

LIPID PROFILE

Total cholesterol, Triglycerides and LDL levels were higher in study group (179.93, 157.43 and 105.97) as compared to control group (162.83, 139.13 and 90.67) which was significant. Whereas HDL level was lower significantly in study group (42.57) as compared to control group (44.63) with (**p< 0.01).(Table3)

The findings of the present study shows obese individuals are at high risk for cardiovascular disorder. According to Assadi Fatemeh et al[75], (2014) the significantly higher value of TC, TGL, LDL and non-significant difference of HDL was observed in obese individuals of BMI>30kg/m2. According to Pallavi et al[27], (2015) the significant higher value of TC, TGL, LDL and significant lower value of HDL was observed in obese individuals but it was at different gender group.

In obesity quality of fat is more important than quantity[75]. Basal plasma FFA concentration is usually elevated in obesity because of increase release of FFA from expanded adipose tissue and decrease FFA clearance. These excess free fatty acids, in plasma enter to liver, primarily increases triglycerides and VLDL which in turn increases LDL and decreases HDL[76].

The increased plasma FFA will inhibit anti-lipolytic effect of insulin and causes further release of FFA. Increase adipocyte mass especially visceral fat, decreases its sensitivity to antil-ipolytic effect of insulin and increases its sensitivity to catecholamine and facilitate lipolysis [51].

CARDIOVASCULAR AUTONOMIC FUNCTION TEST

RESTING HEART RATE VARIABILITY

Heart rate variability is a non-invasive tool to assess ANS. Any alteration in HRV is associated with increased risk of adverse cardiac events. In this study, Resting HRV of 5 minutes was analyzed by using HRV analysis software, university of Kuopio, version 2.2 for both the study group and control group.

TIME DOMAIN MEASURES

Mean HR, Mean RR, SDNN, RMSDD, NN50, pNN50%

Mean HR and Mean RR

The mean HR was increased in study group (75.09±8.00) compared to control group (71.38±5.35) significantly with (*p=0.039). According to Hugh R Peterson et al, heart rate was directly related to body fat percentage.

The heart rate increases due to sympathetic overactivity and reduced parasympathetic activity in obesity[2].

The mean RR interval of study group (810.03 ±85.76) was lower on compared to control group (848.46 ±59.62) and it was statistically significant (*p=0.04). This finding was in accordance with Jaruwaplaengdee et al[77], (2009) that the average RR interval in obese group was lower as compared to non- obese group.

SDNN, RMSDD, NN50 and pNN50%

The standard deviation of the NN intervals (SDNN) is the simplest variable calculated. The SDNN was significantly decreased in the study group (23.17±9.37) as compared to control group (33.33±12.99) with (**p< 0.01). (Table 4) It reflects reduced parasympathetic activity in obesity. There was also a significant decrease in RMSDD, NN50, and pNN50 % in study group as compared to control group with (**p<0.01). This implies in obesity parasympathetic regulation reduced significantly when compared to non-obese individuals.

According to Rajalakshmi et al[78], (2012) SDNN, RMSDD, NN50 and PNN50% were significantly lower in obese group compared to non-obese group. In contrast, Jaruwaplaengdee et al [77], (2009) showed non-significant increased SDNN in obese group and non-significant difference of RMSDD between obese and non-obese group. Obesity, a state of insulin resistance and hyperinsulinemia may decreases cardiac vagal activity and increases cardiovascular risk [38].

FREQUENCY DOMAIN MEASURES

TP, LF nu, HF nu and LF/HF ratio

Total power was decreased in obese group (628.4) as compared to non-obese group (1118.93) which was statistically significant with (*p<0.05) and it is inversely proportional to resting heart rate. It is important to recall that during sympathetic activation the resulting increase in HR is usually accompanied by a marked reduction in total power, whereas the reverse occurs during vagal activation.[46] This is in accordance with findings of G.K pal et al[5] (2014), Rajalakshmi et al[78] (2012), Ravi Kant Soni et al[79] (2014) they all observed decreased total power in obese group as compared to control group.

HF nu was lower in study group as compared to control group significantly with (**p< 0.01).This shows the parasympathetic component was significantly reduced in obesity. LF nu is a marker of sympathetic activity. LF nu was found to be increased significantly in study group as compared to control group with (**p< 0.01).

Representation of LF/ HF in normalized units signifies the balance behavior of two divisions of the autonomic nervous system. LF/HF ratio is an accurate measure of sympathovagal balance. There was significant increase in LF/HF ratio in study group (4.32± 0.97) as compared to control group (2.89±0.54) with (**p< 0.01). (Table 5) This observation was in similar with findings of Anahita R Shenoy et al[80] (2014), GK pal et al[5] (2014), Rajalaksmi et al [78](2014), they all reported significantly decreased HF nu and significantly increased LF nu and LF/HF ratio in obese group.

Significant increased LF nu and decreased HF nu shows definite sympathetic hyperactivity and parasympathetic hypoactivity in obesity. Higher value of LF/ HF ratio indicates sympathovagal balance shifting more towards the sympathetic component in obese group. The higher value of LF/HF ratio also shows more sympathetically driven cardiovascular system in obesity under resting conditions. This increases the work load of the heart by increasing heart rate and peripheral resistance.

Hyperinsulinemia associated with insulin resistance causes sympathetic over activity in obesity. This effect of insulin in long term is maladaptive, because it limits further weight gain and it increases the risk of hypertension, metabolic and cardiac abnormalities.[33] Excess leptin in obesity activates sympathetic nervous system and also increases noradrenaline activity of adrenal medulla[35]. The subclinical inflammation associated with obesity produces inflammatory cytokines such as IL-6, TNF α which also increases sympathetic activity[36], [37]. Thus it implies increase sympathetic activity in obese individuals is mainly is due to hyperinsulinemia or insulin resistance, excess leptin and inflammatory cytokines.

It is well obvious, that the present study shows significantly higher heart rate, LF nu and LF/HF ratio indicating sympathetic predominance in obesity. It also shows significantly lower SDNN, TP and HF nu indicating reduced vagal activity in obesity. The sympathetic stimulation in obese individuals even under resting condition increases heart rate and force of contractions resulting in increased energy consumption and metabolism of cardiac tissue. This increases the production of metabolic waste and

myocardial injuries. Also the blood vessels that are maintained in the sympathetic tone normally, undergoes vasoconstriction due to increase sympathetic activity resulting in hypertension and further consequences in obesity.

DEEP BREATHING TEST

HRV during timed breathing is one of the most reliable and reproducible marker of parasympathetic modulation of cardiac activity. The Deep Breathing is primarily mediated by vagal activity resulting in respiratory sinus arrhythmia (RSA). RSA is a change of heart rate due to respiration induced biochemical changes, intrathoracic pressure changes and central vagal stimulation[81]. It falls under High frequency range of HRV (0.15-0.4 Hz) which is mainly contributed by efferent vagal activity.

In our study, mean HR during deep breathing in study group and control group was almost the same. An increase in SDNN and HF nu in the control group is due to relative increase in vagal activity and decrease in sympathetic activity during slow breathing. The tidal volume increases to compensate reduced breathing rate and to maintain minute ventilation and that is responsible for these autonomic changes. Respiratory sinus arrhythmia was blunted in study group as shown by significant decrease in SDNN and HF nu in study group as compared to control group. (Table 6)

Heart rate increases at inspiration and decreases at expiration. E/I ratio was calculated as the ratio of maximum RR interval during expiration to the minimum RR interval during inspiration at deep breathing (6 breaths per

minute). In this study, there was significant lower value of E/I ratio in study group (1.19 ±0.11) as compared to control group (1.28 ±0.10) indicating decreased parasympathetic activity in obesity with (**p< 0.01) (Table 6). Reduced HRV at one minute controlled deep breathing indicates that cardiac vagal activity and baroreflex response decreases in obesity. According to Chethan et al[82] (2012), E/I ratio was decreased significantly in obese group compared to non-obese group.

VALSALVA MANEUVER

Valsalva ratio was calculated as the ratio of maximum RR interval during phase IV to the minimum RR interval during phase II. In phase IV, due to vagal activity, bradycardia occurs and maximum RR interval is noted. In phase II, due to sympathetic activity and parasympathetic withdrawal, tachycardia occurs and minimum RR interval is noted. Though Valsalva maneuver predict both sympathetic and parasympathetic dysfunction, we are not able to predict the sympathetic component as beat to beat BP monitor is not available in our laboratory. Valsalva ratio was lower in study group (1.32±0.22) as compared to control group (1.47±0.27) significantly with (*p<0.05) (Table 7). This indicates decrease in parasympathetic function and baroreflex activity as body weight increases.

According to Shahin Akhtel et al [38](2008), Rinku Garg[83] et al, E/I ratio and Valsalva ratio were significantly decreased in obese male as compared to normal male. This shows decreased parasympathetic activity and baroreflex response in obesity. The impairment of parasympathetic function in obesity may be due to hyperinsulinemia (or) insulin resistance that causes damage to

microcirculation in many tissue including nerves at level of cardiac muscle or vascular wall. Baroreflex activity may decreases in obesity due to ANS disturbances or altered arterial wall compliance ([38], [83]).

ISOMETRIC HAND GRIP TEST

In response to isometric exercise, rise of systolic and diastolic blood pressure in study group (10.2±2.75,10.8±2.76) were lower as compared to control group(12.27± 4.05, 12.53± 2.87) which was statistically significant with(*p< 0.05) (Table 8). The findings was in accordance with srinath et al [74] (2011), that the base line SBP and DBP were significantly higher in obese group as compared to control group and rise of SBP and DBP in response to isometric exercise were significantly lower in study group as compared to control group. This borderline response to hand grip test is suggestive of reduced sympathetic activity in obesity when subjected to stress.

Cardiovascular responses to (IHGT) are mediated partly by central command and partly by exercising muscle or both. Exercise is a physical stress and is an important activity in daily life. Based on the physical exercise, ANS influence the heart rate and blood pressure. During isometric hand grip exercise in normal person, cardiac sympathetic fibers and peripheral sympathetic fibers gets activated. So there is increase in heart rate and peripheral resistance which results in increasing arterial pressure.

In obesity, there is a borderline rise in pressure due to defect in cardiac sympathetic activation or in peripheral adrenoreceptors during isometric exercise. Thus in obesity there is sympathetic cardiovascular function

derangement in the form of increased resting SBP, DBP and decrease in rise of SBP, DBP in response to isometric hand grip exercise which points out autonomic imbalance. This autonomic imbalance increases cardiovascular risk in obese individuals in later part of their period [70], [84].

CORRELATION OF ANTHROPOEMETRIC INDICES WITH CARDIOVASCULAR AUTONOMIC FUNCTION TEST:

Correlation of Anthropometric Indices with SDNN, TP AND LF/ HF RATIO

BMI and WC shows significant negative correlation with SDNN (-0.336, $p<0.01$), (-0.303, $P<0.05$) and total power (-0.405, $p<0.01$), (-0.347, $p<0.01$) and positive correlation with LF/HF ratio (+0.603, $p<0.01$), (+0.618, $p<0.01$).

WHR also positively correlated with LF/HF ratio (+0.51, $p<0.01$) and negatively correlated with total power (-0.291, $p<0.05$) significantly and with SDNN insignificantly (-0.246, $p=0.058$).

The findings was in accordance with results observed by Rajalakshmi et al[78] (2014), that the anthropometric measurement BMI, WC and WHR was negatively correlated with SDNN and Total power and positively correlated with LF/HF ratio.

Correlation of Anthropometric Indices with E/I Ratio and Valsalva Ratio:

In this study, BMI was negatively correlated with E/ I ratio and Valsalva ratio significantly (-0.44, $p<0.01$), (-0.344, $P<0.01$).

WC and WHR also shows negative correlation with E/ I ratio significantly (-0.433, p<0.01) (-0.424, p<0.01) and Valsalva ratio insignificantly (-0.254, p=0.05) (0.22, P>0.05).

According to Shahin Akhter et al (2008)[38], that BMI and WC were negatively correlated with E/I ratio and Valsalva ratio significantly. Nerella sharvani et al[69] (2015) also observed significant negative correlation of BMI and WHR with E/I and Valsalva ratio in their Studies.

Correlation of Anthropometric Indices with Isometric Hand Grip test:

In our study, BMI was negatively correlated with rise of DBP significantly (-0.262, p<0.05) and rise of SBP insignificantly (-0.207, P>0.05).

WC and WHR also negatively correlated with rise of SBP and DBP though not significant

Kalpana B et al[70] (2015) also noticed negative correlation of BMI and rise in DBP significantly. This shows sympathetic response to isometric exercise decreases as body fat increases.

CORRELATION OF LIPID PROFILE WITH CARDIOVASCULAR AUTONOMIC FUNCTION TEST

Correlation of Lipid Profile with SDNN, TP and LF/ HF RATIO:

In this study, TC, TGL and LDL were positively correlated with LF/HF ratio significantly (+0.53, p<0.01) (+0.488, p<0.01) (+0.582, p<0.01).

TC and LDL also shows negative correlation with SDNN and TP significantly (-0.26, $p<0.05$) (-0.285, $p<0.05$) and (-0.284, $p<0.05$) (-0.322, $p<0.05$)

TGL shows negative correlation with SDNN and TP non-significantly (-0.213, $p>0.05$), (-0.25, $p>0.05$).

HDL shows significant negative correlation with LF/HF ratio (-0.309, $p<0.05$) also correlated positively with SDNN and TP though not significant (+0.142, $p>0.05$), (+0.203, $p>0.05$).

Correlation of Lipid Profile with E/I Ratio and Valsalva Ratio:

In this study, TC and LDL were negatively correlated with E/I ratio and Valsalva ratio significantly (-0.376, $p<0.01$) (-0.405, $p<0.01$) and (-0.297, $p<0.05$) (-0.27, $p<0.05$).

TGL was negatively correlated with E/I ratio significantly (-0.36, $p<0.01$) and Valsalva ratio non-significantly.

Whereas HDL was positively correlated with E/I ratio and Valsalva ratio though not significant.

According to Arunima Chaudhuri et al [85] (2012) TC, TGL and LDL were negatively correlated with E/I ratio and Valsalva ratio. HDL was positively correlated with E/I ratio and Valsalva ratio.

Correlation of Lipid Profile with Isometric Hand Grip test:

TC was negatively correlated with rise of DBP significantly (-0.282, P<0.01) and SBP insignificantly in isometric hand grip exercise.

TGL and LDL were negatively correlated with rise of SBP and DBP but not significant. Whereas HDL was positively correlated with rise of SBP and DBP though not significant.

According to Arunima Chaudhuri et al[86] (2015) TC, TGL and LDL were negatively correlated with isometric hand grip test and HDL was positively correlated with isometric response.

This shows lipids plays a role in modulation of autonomic activity and the autonomic activity decreases in proportion to increase TC, TGL, LDL and decrease HDL. In obesity there is adverse pattern of plasma lipoproteins, high triglycerides, low HDL and abnormal LDL composition. This abnormal lipid profile causes impairment of endothelium dependent arteriolar dilatation in the vessel wall and changes baroreflex capacity. Though elevated LDL is not a component of metabolic syndrome, small dense LDL formed in obesity is highly atherogenic and increases cardiovascular risk. Thus in proportion to increase in LDL, vagal activity and baroreflex capacity reduces which increases coronary artery disease morbidity and mortality in obesity.

CONCLUSION

The present study shows that there is a positive association between higher serum total cholesterol, triglycerides, LDL cholesterol and reduced HDL cholesterol with increased BMI. This is an independent predictor of cardiovascular risk

Cardiovascular autonomic function test in obese male individuals shows

Increase BMI is associated with rise in resting heart rate, blood pressure, LF nu and LF/HF ratio of frequency domain measures of resting HRV in obese group compared to non-obese group. This indicates an increase in the cardiac sympathetic activity at resting conditions in obese individuals

Mean RR, SDNN, RMSSD, NN50 and pNN50% of time domain measures and TP and HF nu of frequency domain measures of resting HRV decrease in obese group compared to non-obese group.

E/I ratio of deep breathing and Valsalva ratio also decreases in obese group compared to non-obese group. This shows decrease in cardiac parasympathetic activity at rest in obese group.

Though sympathetic activity increases in obese males as evidenced by increase baseline HR, BP and LF nu of HRV, the sympathetic response to isometric exercise decreased in obese group which reflects autonomic instability.

All these factors indicates sympathovagal imbalance at rest in obese male individuals in the form of increased sympathetic and decreased parasympathetic activity. This sympathovagal imbalance makes them susceptible to develop cardiovascular dysfunction.

So lipid profile estimation and cardiovascular autonomic function test should be carried out in obesity as early as possible to identify the individuals at risk for cardiovascular disease. Lifestyle modification in the form of regular exercise, practicing yoga and also dietary modification are suggested to reduce the weight and to shift the sympathovagal balance in favour of vagal predominance to prevent cardiovascular dysfunction in obesity.

Limitation

To find the risk of metabolic syndrome in apparently healthy obese individual's insulin resistance and glucose tolerance test is to be carried out.

Studies based on duration of obesity and effect of weight loss on cardiac autonomic activity is to be carried out.

Effect of obesity on cardiac autonomic activity can be studied more significantly by evaluating insulin resistance and leptin level

SUMMARY

The study aims at evaluation and comparison of lipid profile and cardiovascular autonomic function in obese male individuals with that of healthy normal individuals of age group 25-40 years.

The following Autonomic function tests were performed.

1. Heart rate variability at supine rest
2. Heart rate changes at one minute controlled deep breathing (E/I RATIO)
3. Heart rate changes during Valsalva maneuver
4. Blood pressure response to Sustained isometric handgrip exercise.

The following results were obtained:-

Lipid profile estimation shows significant increase in serum TC, TGL, LDL and decrease HDL in obese male.

Autonomic function test shows

Significant increase in the resting heart rate.

Significant reduction in SDNN and HF nu in resting HRV indicating parasympathetic withdrawal.

Significant increase in the LF nu and LF/HF ratio indicates sympathetic over activity under resting conditions.

Also shows decrease in E/I ratio of Deep Breathing and Valsalva Ratio of Valsalva maneuver which implies reduced parasympathetic function and baroreflex activity in obesity.

Decrease in rise of SBP and DBP in response to Sustained isometric handgrip exercise shows reduced sympathetic activity at stress and autonomic instability in obesity.

Cardiovascular autonomic function, when tested using standard autonomic function tests were significantly altered in obese male individuals. Hence autonomic function tests including HRV may be used as a tool to diagnose autonomic dysfunction earlier. This to take effective measures earlier to prevent obesity associated morbidity and mortality.

BIBILIOGRAPHY

1. Madhuri Sharma. Childhood Obesity and Cardiovascular Autonomic Nervous System. International Journal of Basic and Applied Physiology. 2012 ;Vol 1(1) :pp171-174

2. Kanavi Roopa Shekharappa , Smilee Johncy S , Mallikarjuna P T , Vedavathi K J et al. Correlation between body mass index and cardiovascular parameters in obese and non- obese in different age group. Int J Biol Med Res. 2011; 2(2): 551-555.3.

3. Rupali S. Baburdikar, Ravindra S. Inamdar. Comparative study of Anthropometric Measurements & Lipid Profile in Cardiovascular Disease Risk Factors. Journal of Evidence Based Medicine and Healthcare. 2015 September 07; Volume 2 Issue 36: pp 5630-5639.

4. Arunima Chaudhuri, Amit Kumar Bandopadhyay et al. Obesity, A Burning Problem. IOSR Journal of Pharmacy. (January 2014); Volume 4 : pp 01-05.

5. Jagadeeswaran Indumathy Pravati Pal, Gopal Krushna Pal, Tarun Kumar Dutta et al. Assessment of heart rate variability indices in overweight and obese Indian population. International Journal of Clinical and Experimental Physiology. 2014; Volume 1: pp192-195.

6. Kismat Mohammad Turki , Mohammad Hadi Alosami , Zina Hasan Abdul-Qahar. The Effect of Obesity on Serum Leptin and Lipid Profile. The Iraqi Postgraduate Medical Journal. 2009 ; VOL.1: NO. 129

7. Kannel WB , Plehn JF, Cupples LA et al. Cardiac failure and sudden death in the Framingham Study. Am Heart J. 1988 Apr; 115(4): pp 869-75.

8. David A.Warrell, Timthy M. cox .Oxford Text book of Medicine. Fifth Edition. Oxford university press. 2010;volume1: pp1527-1531 and1652-1660.

9. Racette SB, Deusinger SS, Deusinger RH et al. Obesity: overview of prevalence, etiology, and treatment. Phys Ther. 2003; 83: 276 –288.

10. WHO/IASO/IOTF. The Asia-Pacific perspective: redefining obesity and its treatment. Health Communications Australia: Melbourne, 2000.

11. Sholomomelmed Kenneth S.polonosky .Williams Text Book of Endocrinology. Elsevier.12th Edition.2012; Chapter36: pp1605-1618.

12. Deepa M, Farooq S, Deepa R ,Manjula D and Mohan V et al. Prevalence and significance of generalize and central body obesity in an urban Asian Indian population in Chennai, India (CURES: 47). European Journal of Clinical Nutrition. 2009; 63: pp 259–267.

13. Harrison's Principles of Internal Medicine Textbook . Eighteenth Edition. Mc Grawhill companies.2012; Volume 1 & 2: Chapter 77 p622-635& Chapter 356 pp3143-3147.

14. Guyton C, John E. Hall. Guyton Textbook of Medical physiology. Eleventh Edition. Elsevier. 2007; Chapter 71: pp 865-873

15. Jéquier E . Leptin Signaling, Adiposity and Energy Balance. Annals of the New York Academy of Sciences. 2002 ; 967: pp 379–388.

16. Zhang JV, Ren PG, Avsian-Kretchmer O, Luo CW, et al. Obestatin, a peptide encoded by the ghrelin gene, opposes ghrelin's effects on food intake. Science. 2005 Nov 11; 310(5750): pp 996-999.

17. Ganong wf, Review Of Medical Physiology. 23rd Edition .McGraw Hill; 2005.

18. Bouchard C, Tremblay A. Genetic Effects In Human Energy Expenditure Components. Int J Obes.1990 ;14 (Suppl 1):pp 49–55.

19. Stephen O'rahilly and sadaf farooqi I .Human Obesity: A Heritable Neurobehavioral Disorder that is highly sensitive to environmental conditions. Diabetes. nov (2008); vol 57: 2905-2909.

20. Tatiana Gurevich-Panigrahi, Soumya Panigrahi, Emilia Wiechec, et al. Obesity: Pathophysiology and Clinical Management .Current Medicinal Chemistry .2009 ;Vol 16: No. 1.

21. Segal Nl, Allison Db. Twins And Virtual Twins: Bases Of Relative Body Weigh Revisited. Int J Obes. 2002 ; 26: 437–441.

22. Hill JO, Peters JC. Environmental Contributions To The Obesity Epidemic. Science. 1998 May 29; 280(5368):1371-4.

23. Qazi Iqbal Ahmad . Childhood Obesity. Indian J Endocrinol Metab. 2010 Jan-Mar; Volume 14: pp 19-25.

24. Miyashita Y , Shirai K, Itoh Y, Sasaki H,et al. Low Lipoproteinlipase Mass In Preheparin Serum Of Type 2 Diabetes Mellitus Patients And Its Recovery With Insulin Therapy. Diabetes Res Clin Pract. 2002 Jun; 56(3):181-7.

25. Tchernof A, Lamarche B, Prud'Homme D, Nadeau A, Moorjani Set al.The dense LDL phenotype. Association with plasma lipoprotein levels, visceral obesity, and hyperinsulinemia in men. Diabetes Care. 1996 Jun; 19(6): pp 629-37.

26. Tabas I1, Williams KJ, Borén J. et al. Subendothelial lipoprotein retention as the initiating process in atherosclerosis: update and therapeutic implications. Circulation 2007 Oct 16; 116(16): pp 1832-44.

27. Pallavi S. Kanthe , Bheemshetty S. Patil , Shrilaxmi Bagali et al. Atherogenic Index as a Predictor of Cardiovascular Risk among Women with Different Grades of Obesity, International Journal of Collaborative Research on Internal Medicine & Public Health.(2012) ;Vol. 4: pp1767 -1774.

28. M. Grundy, J. I. Cleeman, S. R. Daniels et al “Diagnosis And Management Of The Metabolic Syndrome: An American Heart Association/National Heart, Lung, And Blood Institute Scientific Statement,” Circulation. 2005 October 25; vol. 112 :no. 17.

29. Bill Blessing and Ian Gibbins. Autonomic Nervous System. Scholarpedia. 2008 ;3(7)

30. Laitinen T Autonomous Neural Regulations physiology and maintenance vol5.

31. Dampney R A, Horiuchi J, Tagawa T, et al. Medullary And Supramedullary mechanisms Regulating Sympathetic Vasomotor Tone. Acta Physio Scand.2003;177: pp209-218 .

32. Landsberg L. Obesity, Metabolism, and Hypertension. Yale J Biol Med. 1989 Sep-Oct; 62(5): pp 511–519.

33. EmdinM, Gastaldelli A, Muscelli E et al. Hyperinsulinemia and Autonomic nervous system dysfunction in obesity: Effects of weight loss. Circulation. 2003; 103: pp 513–9.

34. Juan-Manuel Guízar, Rosalía Ahuatzin, Norma Amador, Guillermo Sánchez and Gustavo Romer et al. Heart Autonomic Function in Overweight Adolescents. indian pediatrics. 2005 MAY 17 ; VOLUME 42: pp 464-468

35. Christopher L. Kaufman, Daniel R. Kaiser, JuliaSteinberger, Aaron S. Kelly, and Donald R.Dengel R.W.Lucky. Relationships of Cardiac Autonomic Function With Metabolic Abnormalities in Childhood Obesity. Obesity (Silver Spring). 2007 May; 15(5): pp1164-71.

36. Gallistl S, Sudi KM, Aigner R Borkenstein M. Changes in serum interleukin-6 concentrations in obese children and Adolescents during a weight reduction program. Int J Obes Relat Metab Disord. 2001; 25: pp 1640 –3.

37. Tarek Mohamed Ali, Ahmad Abdelhakam E,Askary. Association of heart rate variability indices with inflammatory markers in nondiabeticobese dyslipidemic middle agedSaudi population .2014 ;Volume 1 Issue : 2 : pp 135-141

38. Shahin Akhter,Noorzahan Begum, Sultana Ferdousi, Shelina Begum,Taskina Ali. Relationship Between Obesity And Parasympathetic Nerve Function. J Bangladesh Soc Physiol. 2008 Dec; (3) : pp 50-54

39. Ioanna Skrapari, Nicholas Tentolouris, Despoina Perrea, Christos Bakoyiannis et al. Baroreflex Sensitivity in Obesity. Relationship With Cardiac Autonomic Nervous System Activity. OBESITY July 2007; Vol. 15 No. 7: pp 1685-1692

40. Yudkin Js, Kumari M, Humphries Se, Mohammed-Ali V. Hand book of obesity-. Inflammation, Obesity, Stress And Coronary Heart Disease: Is Interleukin-6 And The Risk Of Future Myocardial Infarction Among Apparently Healthy Men Circulation 2000; 101: pp 1767-1772.

41. Esler M, Jennings G, Korner P, Blombery P, Sacharias N ,Leonard et al. Measurement of total and organ specific norepinephrine kinetics in humans. American Journal of Physiology Endocrinology and Metabolism. July 1984 ; Vol. 247 : no. 1.

42. Ewing DJ, Martyn CN, Young RJ, Clarke BF. The value of cardiovascular autonomic function tests: 10 years' experience in diabetes. Diabetes Care. 1985 Sep-Oct; 8(5): pp 491-8.

43. Chhaya Ahire, Varsha Sarode , Kiran kumar Jadhav, Veena Shriram, Nishi Gaidhani. Prevalence of Cardiac Autonomic Neuropathy in short and long standing type II diabetics in western Maharashtra Indian Journal of Basic and Applied Medical Research. .September 2014; Vol.-3: P. 252-9.

44. Assessment: Clinical Autonomic Testing Report of the Therapeutics and Technology Assessment Subcommittee. American Academy of Neurology.1996: pp1-10.

45. Christopher G Goetz, Eric J pappert. Text book of Clinical Neurology. First Edition by W.B Sanders company.1999; chapter21: pp350-561.

46. Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology 1996 Heart rate variability: standards of measurement. physiological interpretation and clinical use. Circulation 93:1043–1065.

47. Jong Weon Choi1 et al. Associations Between Total Body Fat and Serum Lipid Concentrations in Obese Human Adolescents. Ann Clin Lab Sci Summer. 2002 ; vol. 32 no. 3: pp 271-278.

48. Walton C1 et al. Body fat distribution, rather than overall adiposity, influences serum lipids and lipoproteins in healthy men independently of age. Am J Med. 1995 Nov; 99(5): pp 459-64.

49. Stephen R et al .Association of Body Fat Distribution and Cardiovascular Risk Factors in Children and Adolescents Circulation. 1999; 99: pp 541-545.

50. SavvaS C et al. Waist circumference and waist-to-height ratio are better predictors of cardiovascular disease risk factors in children than body mass index. International Journal of Obesity. November 2000; Volume 24: Number 11 pp 1453-1458.

51. Guenther Boden et al. Obesity and Free Fatty Acids (FFA) .Endocrinol Metab Clin North Am. 2008 Sep; 37(3): pp 635–9

52. Carey N. et al .Inflammatory links between obesity and metabolic disease. J Clin Invest. 2011 Jun 1; 121(6):pp 2111–2117.

53. Zohreh mazloom et al .Effect of obesity on inflammation and lipid profile of obese women. Saudi med ej. 2009; vol 30(10):pp 1357-58.

54. Luisa Soares-Miranda et al.Central Fat Influences Cardiac Autonomic Function in Obese and Overweight Girls. Pediatr Cardiol . 2011 Oct; 32(7): pp 924-8.

55. Arone LJ et al. Autonomic nervous system activity in weight gain and weight loss. Am J Physiol. 1995 Jul; 269(1 Pt 2):R222-5.

56. Bernd Fruehwald- Schultes et al .Supraphysiological Hyperinsulinemia Acutely Increases Hypothalamic-Pituitary-Adrenal Secretory Activity in Humans. The Journal of Clinical Endocrinology & Metabolism. July 01, 2013; Volume 84: Issue 9.

57. Urs Scherrer et al. Body Fat and Sympathetic Nerve Activity in Healthy Subjects. Circulation. 1994; 89: pp 2634-2640.

58. Mariovaz MD et al Regional Sympathetic Nervous Activity and Oxygen Consumption in Obese Normotensive Human Subjects. Circulation. 1997; 96: Pp 3423-3429.

59. Kazuko Masuo et al. Weight Gain–Induced Blood Pressure Elevation. Hypertension. 2000; 35: 1135-1140.

60. Shahin Akhter, Noorzahan Begum, Sultana Ferdousi , Sakhawat,Mahmud Khan. Autonomic Neuropathy in Obesity. J Bangladesh Soc Physiol. 2011 June; 6(1): pp 5-9 .

61. Chin-Hua Fu1, Cheryl C. H. Yang Chin-Lon Lin,and Terry B. J. Ku Alteration of Cardiovascular Autonomic Functions by Vegetarian Diets in Postmenopausal Women Is Related to LDL Cholesterol Levels Chinese Journal of Physiology. 2008; 51(2) : pp 100-105.

62. Bootsma M et al. Heart rate and heart rate variability as indexes of sympathovagal balance .American Journal of Physiology - Heart and Circulatory Physiology. Published 1 April 1994; Vol. 266 no. 4 : H1565-H1571 .

63. Hayano J et al. Accuracy of assessment of cardiac vagal tone by heart rate variability in normal subjects. Am J Cardiol. 1991 Jan 15; 67(2): pp 199-204.

64. Piccirillo G et al. Heart rate and blood pressure variability in obese normotensive subjects. Int J Obes Relat Metab Disord. 1998 Aug; 22(8): pp 741-50.

65. Michikazu Sekine et al. Obesity and cardiac autonomic nerve activity in healthy children: Results of the toyama birth cohort study. Environ Health Prev Med. 2001 Oct; 6(3): 149–1531.

66. Standard of medical care in diabetes. Diabetes care. 2014; volume 37: supplement1

67. Executive summary of the third report of the NCEP expert panel on detection. Evaluation and treatment of high blood cholesterol in adults

68. Simran Grewal, Vidushi Gupta et al. Effect of obesity on autonomic nervous system. Int J Cur Bio Med Sci. 2011; 1(2): pp 15 – 18.

69. Nerella Sharvani R. Nasar Ahameda. Study of Autonomic Functions and Obesity in Postmenopausal Women. April 2015; Volume 4 Issue 4: pp307-309.

70. B Kalpana1et al. Study of sympathetic nerve activity in young Indian obese individuals Year. Archives of Medicine and Health Sciences. 2013 ; Volume 1: pp 29-32

71. Hirsch J . Heart rate variability as a measure of autonomic function during weight change in humans. Am J Physiol. 1991 Dec;261 (6 Pt 2): R1418-23.

72. Ravikeerthy.M, Tejaswi Nataraj . A Comparative Study of Cardiovascular Parameters in Obese and Non-Obese Individuals. International Journal of Scientific and Research Publications. May 2015; Volume 5: Issue 5 p 1-5.

73. Ajay K T, Vatsala A.R, Suresh Y Bondade, Sonam D, Sangam. Effect of Obesity on Cardiovascular Functions in Adolescent Male. J. Pharm. Sci. & Res. 2014;Vol. 6(3): pp 164-166.

74. Srinath.C.Ga & Ravipati Sarath. Cardiovascular Response to Isometric Handgrip Exercice Test in Obese and Normal Weight Young Adults. IJBR. 2011; 2[11]: 554-560.

75. Assadi Fatemeh and Nooraei Farahnaz. Lipid profile Markers in Obese and Normal Weigh Individuals and their Relation with Obesity Determinants .Biological Forum – An International Journal . 2014; 6(2): pp 514-518.

76. Surajit Kumar Mukhopadhyay et al. Study of Lipid Profile in Obese Individuals and the Effect of Cholesterol Lowering Agents on them. Al Amle en J Med S c i. 2 012; 5 (2) : pp 1 4 7 -1 5 1.

77. Jaruwan Plaengdee Wilaiwan Khrisanapant. Effects Of Obesity On Cardiac Autonomic Activity In Adult. National graduate research conference. 2009 feb; pp 1336 -1342 .

78. Rajalakshmi R, VijayaVageesh Y, Nataraj SM, MuraliDhar, Srinath CG. Heart Rate Variability In Indian Obese Young Adult. Pak J Physiol .2012; 8(1): pp39-44.

79. Ravi Kant Soni, Jyotsna Shukla, Amitabh Dube, Arvind Kumar Shukla, Ranjeeta Soni. A Comparative Study of Heat Rate Variability in Obese and Healthy YoungAdults (18 – 25 Years). RJPBCS. 2014 May-June; 5(3): pp1111-14.

80. Anahita R Shenoy et al. Impact Of Obesity On Cardiac Autonomic Functions In Middle Aged Males. National Journal of Physiology, Pharmacy & Pharmacology. 2014; Vol 4 Issue 3 pp 236 – 239.

81. P. Zhang, W. Tapp, S. Reisman, B. Natelson. ―Respiration Response Curve Analysis of Heart Rate Variability, IEEE Trans. Biomed Eng. April 1997; 44(4):321-325.

82. Chethan HA, Niranjan Murthy, Basavaraju K. Comparative study of heart rate variability in normal and obese young adultmales. Int J Biol Med Res. 2012; 3(2): 1621-1623

83. Rinku Garg, Varun Malhotra, Neera Goel, Usha Dhar, Yogesh Tripathi. A Study Of Autonomic Function Tests In Obese People. Int J Med Res Health Sci. 2013; 2(4): pp 750-755

84. Khwaja Nawazuddin Sarwari1, Moin Sabeer, Mohammed Imran and Arshiya Zeba. Comparison of Autonomic Cardiovascular Functions using Heart Rate Variability Test In Young Obese And Non-Obese

Males And Females An Online International Journal Available at http://www.cibtech.org/cjs.htm. 2013 September-December; Vol 2 (3). pp.75-80.

85. Arunima Chaudhuri, Nirmala Gopal Borade, Sudipta Saha. Relationship of Gender and Lipid Profile with Cardiac Parasympathetic Reactivity. Journal of Basic and Clinical Reproductive Sciences .2012 January - December ; Vol 1 : Issue 1 and 2.

86. Arunima Chaudhuri, Nirmala Gopal Borade, Amit K. Bandopadhyay, Samir K. Hazra, Sudipta Saha. A comparative study of lipid profile and autonomicfunctions in vegetarian and non-vegetarian postmenopausal women. Medical Journal of Dr. D.Y. Patil University. 2013 January-March. Vol 6. Issue 1.

ANNEXURES

APPENDIX - A

Name **Height**

Age **Weight**

Sex **Occupation**

No.	Autonomic Symptoms		Yes	No.
1.	Nasal symptoms	a. drynose b. running nose		
2.	Sweating symptoms	a. Increased b. Decreased		
3.	Postural fall/dizziness on standing			
4.	GIT Symptoms	a. Diarrhoea b. Constipation d. Discomfort/pain		
5.	Headache/Migraine / (Heaviness of head throbbing headache)			
6.	Micturition disturbances	a. Frequency b. Urgency c. Incontinence d. Nocturia e. Hesitancy		

7.	Occasional attacks of bronchospasm (after exercise, laughter, or emotion)					
8.	Do u feel hot or cold					
9.	Do your extremities remain		a. Warm b. Cold			
10.	Burning feet					
11.	Risk factors		a. Obesity b. Hypertension c. Diabetes Mellitus d. CHD e. Smoking f. Alcoholism			
12.	Any stress related physical symptoms (flushing, choking, laump in the throat, general weakness)					
13.	Any other general symptoms					
14.	Allergy to any drug					
14.	Physical status	Regular athlete	Occ.player/ sedentary	Regular exercise		

	HRV5 min SUPPINE REST	ONE MINUTE CONTROLLED DEEP BREATHING
Time domain measures	Mean HR Mean RR SDNN RMSSD NN50 pNN50	SDNN
Frequency domain measures	Total power LFnu HFnu LF/HF Ratio	HFnu
		E/I Ratio Max RR Interval Min RR Interval
Valsalva Ratio Max RR Interval Min RR Interval		
Isometric Hand Grip Systolic BP Difference Diastolic BP Difference.		

PATIENT CONSENT FORM

STUDY DETAIL :

"EVALUATION OF CARDIO VASCULAR RISK IN OBESE INDIVIDUALS BASED ON LIPID PROFILES AND AUTONOMIC FUNCTION"

STUDY CENTRE:

Department of Physiology & Medicine op, Chengalpattu Medical College & Hospital, Chengalpattu.

PATIENT NAME: **AGE:** **SEX:**

IDENTIFICATION NUMBER:

I confirm that have understood the purpose of procedure for the above study.

I have the opportunity to ask question and all my questions and doubts have been answered to my satisfaction.

I understand that my participation in the study is voluntary and that I am free to withdraw anytime without giving any reasons, without my legal rights being affected.

I understand that my investigator, regulatory authorities and the ethics committee will not need my permission to look at my health records both in respect to the current study and any further research that may be conducted in relation to it, even if I withdraw from the study, I understand that my identity will not be revealed in any information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arrives from the study.

I agree to take part in the above study and to comply with the instructions given during the study and faithfully cooperate with the study team.

I hereby give consent to participate in this study.

I hereby give permission to undergo complete clinical examination and diagnostic test.

Signature of investigator

Signature/Thumb impression of participant

Date:
Place:

Participant's address:

ஆராய்ச்சியின் ஒப்புதல் கடிதம்

ஆராய்ச்சியின் தலைப்பு

பெயர் : நேதி :

வயது :

பால் : ஆராய்ச்சி சேர்க்கை எண் :

இந்த ஆராய்ச்சிகளும் அதன் விவரங்களும் எனக்கு முழுமையாக விளக்கப்பட்டது

எனக்கு விளக்கப்பட்ட விவரங்களை புரிந்துக் கொண்டு நான் என்னுடைய சம்மதத்தை தெரிவித்தேன்.

இந்த ஆராய்ச்சியில் நான் என்னுடைய சொந்த விருப்பத்தின் பேரில் பங்கேற்கிறேன். இந்த ஆராய்ச்சியிலிருந்து எந்நேரமும் விலகிக்கலாம் என்றும் அதனால் எவ்வித பாதிப்பும் ஏற்படாது என்பதையும் நான் புரிந்து கொண்டேன். எனக்கு கருப்படம் (சிசிடி) எடுக்க சம்மதம்

நான் இந்த ஆராய்ச்சியின் விவரங்களை கொண்ட தகவல்களை பெற்றுக் கொண்டேன்.

நான் என்னுடைய சுய நினைவுடனும் மற்றும் முழு சுதந்திரத்துடனும் என்னை இந்த ஆராய்ச்சியில் ஈடுபட சம்மதிக்கிறேன்.

நான் கொழுப்பு சத்து பார்க்க என்னுடைய உடம்பிலிருந்து இரத்தம் எடுக்க சம்மதிக்கிறேன்.

கையொப்பம்

MASTER CHART

ANTHROPOMETRIC CHARACTERISTIC, LIPID PROFILE AND

BASELINE BLOOD PRESSURE IN STUDY GROUP

S.No	AGE in years	WTK g	HT cm	HT m	BMI kg/m^2	WC cm	HC cm	WHR	TC mg/dl	TGL mg/dl	HDL mg/dl	LDL mg/dl	SBP mmHg	DBP mm Hg	PP mm Hg	MAP mm Hg
O1	33	82	162	1.62	31	91	96	0.94	199	169	44	121	118	74	44	88.67
O2	37	87	162	1.62	33	92	97	0.94	195	177	44	116	122	74	48	90
O3	39	82	165	1.65	30	92	99	0.92	198	172	42	122	126	80	46	95.33
O4	35	76	161	1.61	29	91	99	0.91	176	157	43	102	124	76	48	92
O5	32	78	164	1.64	29	91	97	0.93	171	158	42	100	120	76	44	90.67
O6	32	90	176	1.76	29	91	99	0.91	186	169	41	111	120	70	50	86.67
O7	34	87	167	1.67	31	93	100	0.93	192	172	41	117	120	72	48	88
O8	34	82	165	1.65	30	91	95	0.95	179	163	40	104	120	78	42	92
O9	36	77	161	1.61	29	89	95	0.93	185	165	42	110	118	74	44	88.67
O10	32	79	166	1.66	28	87	95	0.91	169	144	39	101	114	70	44	84.67
O11	35	82	166	1.66	29	92	97	0.94	180	166	40	105	118	74	44	88.67
O12	31	91	178	1.78	28	92	96	0.95	189	163	43	114	116	68	48	84
O13	32	72	157	1.57	29	87	93	0.93	170	149	42	98	114	78	36	90

S.No	AGE in years	WTK g	HT cm	HT m	BMI kg/m^2	WC cm	HC cm	WHR	TC mg/dl	TGL mg/dl	HDL mg/dl	LDL mg/dl	SBP mmHg	DBP mm Hg	PP mm Hg	MAP mm Hg
O14	34	82	167	1.67	29	90	99	0.9	174	154	44	99	122	80	42	94
O15	35	74	167	1.67	26	87	95	0.91	164	142	41	95	118	76	42	90
O16	36	78	162	1.62	29	92	99	0.92	186	162	41	113	120	74	46	89.33
O17	34	86	170	1.7	29	91	101	0.9	173	149	43	100	126	82	44	96.67
O18	33	76	164	1.64	28	90	101	0.89	180	152	42	108	122	80	42	94
O19	34	82	166	1.66	29	92	91	1.01	190	174	42	113	124	78	46	93.33
O20	29	76	161	1.61	29	88	96	0.91	177	155	44	100	128	80	48	96
O21	30	97	179	1.79	30	91	97	0.93	188	165	47	110	114	72	42	86
O22	36	80	170	1.7	27	89	94	0.94	172	149	42	100	120	78	42	92
O23	35	73	162	1.62	27	85	90	0.94	175	150	44	101	118	78	40	91.33
O24	32	76	160	1.6	29	87	95	0.91	188	145	45	114	120	72	48	88
O25	38	81	165	1.65	29	89	96	0.92	190	153	43	117	128	84	44	98.67
O26	33	68	157	1.57	27	85	94	0.9	170	148	44	97	126	78	48	94
O27	34	71	156	1.56	29	91	97	0.93	185	164	41	111	122	80	42	94
O28	29	72	167	1.67	25	86	95	0.9	164	142	45	91	116	70	46	85.33
O29	30	78	165	1.65	28	90	99	0.9	173	152	44	99	128	82	46	97.33
O30	28	81	175	1.75	26	83	92	0.9	160	143	42	90	114	74	40	87.33

ANTHROPOMETRIC CHARACTERISTIC, LIPID PROFILE AND BASELINE BLOOD PRESSURE IN CONTROL GROUP

S.NO	AGE in years	WT Kg	HT cm	HT m	BMI kg/m^2	WC cm	HC cm	WHR	TC mg/dl	TGL mg/dl	HDL mg/dl	LDL mg/dl	SBP mm Hg	DBP mmHg	PP mm Hg	MAP
C1	30	64	164	1.64	23	80	92	0.86	172	147	47	96	120	84	36	96
C2	32	54	169	1.69	18	72	84	0.85	146	133	41	80	118	74	44	88.67
C3	34	62	169	1.69	21	74	86	0.86	154	118	47	83	116	70	46	85.33
C4	39	54	165	1.65	19	72	83	0.86	147	115	43	81	122	80	42	94
C5	30	70	169	1.69	24	83	95	0.87	179	154	48	100	126	82	44	96.67
C6	31	70	172	1.72	23	85	92	0.92	179	161	40	107	118	78	40	91.33
C7	35	62	162	1.62	23	78	89	0.87	157	126	47	85	108	70	38	82.67
C8	33	54	160	1.6	21	72	83	0.86	153	127	46	82	96	62	34	73.33
C9	32	65	167	1.67	23	86	91	0.94	181	162	47	102	114	68	46	83.33
C10	36	58	158	1.58	23	82	92	0.89	168	147	42	97	106	76	30	86
C11	28	64	164	1.64	23	78	88	0.88	161	140	44	89	124	76	48	92
C12	30	68	170	1.7	23	78	89	0.87	167	144	45	93	106	66	40	79.33
C13	29	58	160	1.6	22	77	86	0.89	160	142	42	90	114	68	46	83.33
C14	30	62	169	1.69	21	76	87	0.87	166	145	48	89	120	84	36	96
C15	34	68	169	1.69	23	80	88	0.9	167	141	43	96	120	76	44	90.67
C16	36	67	170	1.7	23	85	92	0.92	179	157	45	103	108	76	32	86.67

S.NO	AGE in years	WT Kg	HT cm	HT m	BMI kg/m^2	WC cm	HC cm	WHR	TC mg/dl	TGL mg/dl	HDL mg/dl	LDL mg/dl	SBP mm Hg	DBP mmHg	PP mm Hg	MAP
C17	38	54	162	1.62	20	73	84	0.86	146	126	41	80	114	62	52	79.33
C18	34	67	171	1.71	22	76	86	0.88	161	137	44	90	104	60	44	74.67
C19	35	57	170	1.7	19	72	83	0.86	159	119	52	84	110	74	36	86
C20	29	66	167	1.67	23	84	94	0.89	169	148	41	97	112	78	34	89.33
C21	30	60	174	1.74	19	74	84	0.88	152	127	45	81	90	58	32	68.67
C22	29	61	165	1.65	22	74	84	0.88	157	125	44	88	118	70	48	86
C23	33	67	171	1.71	22	74	86	0.86	162	135	46	89	114	78	36	90
C24	35	68	169	1.69	23	84	95	0.88	175	153	45	100	98	62	36	74
C25	29	60	170	1.7	20	72	84	0.85	153	126	44	84	114	66	48	82
C26	30	61	163	1.63	22	76	84	0.9	164	139	42	94	110	66	44	80.67
C27	33	70	171	1.71	23	82	95	0.86	162	142	45	89	118	76	42	90
C28	31	56	168	1.68	19	76	86	0.88	152	134	45	84	118	70	48	86
C29	34	65	167	1.67	23	81	94	0.86	174	149	47	97	116	70	46	85.33
C30	32	63	168	1.68	22	77	89	0.86	163	151	43	90	110	72	38	84.67

HRV IN SUPINE REST-STUDY GROUP

S.no	MEAN HR bpm	MEAN RR ms	SDNN ms	RMSSDN ms	NN50	pNN50 (%)	Total power	LF/HF	LF nu	HF nu
O1	72.41	830.5	26.1	18.1	14	3.9	348	4.837	82.8	17.1
O2	79.06	759.2	9.6	6.4	0	0	94	4.065	80.2	19.7
O3	88	684.1	22.1	13.9	9	2.1	327	6.433	86.5	13.4
O4	78.86	764.5	32.65	24.25	28	7.12	1187	4.6318	82.133	17.73
O5	77.67	773.5	18.3	13.2	8	2.1	113	3.618	78.3	21.6
O6	73.52	817.2	19.1	14.4	4	1.1	289	4.308	81.1	18.8
O7	71.87	836	17.4	11.6	2	0.6	281	4.386	81.4	18.6
O8	68.03	884.2	30.7	25.1	23	6.8	520	3.326	76.8	23.1
O9	66.54	902.6	15.9	13.1	4	1.2	260	4.152	80.4	19.4
O10	65.38	918.7	20	17.4	7	2.1	155	4.201	80.6	19.2
O11	65.29	920.9	26.3	21.2	13	4	585	3.581	78	21.8
O12	63.7	945.3	27.3	20.8	14	4.4	775	5.185	83.8	16.2
O13	61.92	970.7	25.7	20.8	16	5.2	643	3.748	78.8	21
O14	72.13	835.9	36.9	28.9	26	7.3	1343	4.451	81.5	18.3
O15	70.06	859.6	27.7	20.8	22	6.3	1003	3.929	79.7	20.3

S.no	MEAN HR bpm	MEAN RR ms	SDNN ms	RMSSDN ms	NN50	pNN50 (%)	Total power	LF/HF	LF nu	HF nu
O16	65.56	922.2	43.8	33.7	33	10.2	2100	5.026	83.3	16.6
O17	83.84	717.1	22.5	15.8	11	2.6	302	2.713	73.1	26.9
O18	77.69	773.1	16.4	12.2	5	1.3	358	4.653	82.2	17.7
O19	79.97	751.3	13.6	9.2	3	0.8	95	4.746	82.6	17.4
O20	86.33	696.5	16.4	11.2	1	0.2	219	2.815	73.8	26.2
O21	71.9	836	24.9	19	14	3.9	790	4.375	81.3	18.6
O22	88.7	678.5	24.4	17.7	16	3.6	683	2.836	73.9	26.1
O23	75.64	797.2	53.1	44.5	36	9.6	4057	4.004	80	20
O24	66.68	900.8	18.6	13.7	5	1.5	342	5.389	84.3	15.6
O25	83.34	720.8	19.9	13.1	8	1.9	410	6.516	86.6	13.3
O26	89.86	668.1	10.2	7.5	0	0	103	2.954	74.6	25.3
O27	81.84	735.7	14.3	9.7	2	0.5	230	4.751	82.6	17.4
O28	71.13	844.2	18	14.1	4	1.1	340	3.934	79.7	20.2
O29	81.9	741.2	23.5	16	11	2.7	604	5.958	85.6	14.4
O30	73.93	815.3	19.7	13.7	6	1.6	296	4.021	80.1	19.9

HRV IN SUPINE REST-CONTROL GROUP

S.No	MEAN HR bpm	MEAN RR ms	SDNN ms	RMSSDN ms	NN50	p NN50 (%)	Total power	LF/HF	LF nu	HF nu
C1	73.94	813.3	24	18.1	13	3.5	676	3.171	76	24
C2	69.72	861.3	18.7	15.2	10	2.9	409	3.252	76.4	23.5
C3	68.43	877.6	18.7	14.4	7	2	546	4.122	78.4	19.5
C4	74.6	805.5	23.5	19	11	3	503	2.956	74.6	25.2
C5	63.68	949.8	58.4	46.7	32	10.2	2567	1.991	66.5	33.4
C6	77.56	777.9	48.9	38.3	47	12.2	2184	3.174	76	23.9
C7	69.98	859.2	25.3	19.9	13	3.7	526	3.459	77.5	22.4
C8	71.92	842.6	41.3	32.3	34	9.6	1559	3.29	76.7	23.3
C9	68.43	878	22.9	18.2	10	2.9	790	2.562	71.9	28.1
C10	64.98	926	26	21.5	15	4.6	1013	3.08	75.5	24.5
C11	72.58	834.4	45.1	35.1	40	11.1	1717	2.194	68.6	31.3
C12	83.28	721.5	19.7	14.8	8	1.9	300	2.352	70.2	29.8
C13	68.8	875.4	46.3	39.9	49	11.8	1290	3.336	76.7	23
C14	82.16	736.2	34.9	25.6	26	6.4	1165	3.127	75.8	24.2
C15	86.22	697	17.3	12.3	1	0.2	232	1.47	59.5	40.5

S.No	MEAN HR bpm	MEAN RR ms	SDNN ms	RMSSDN ms	NN50	p NN50 (%)	Total power	LF/HF	LF nu	HF nu
C16	65.26	920.7	19.4	16.5	14	4.3	289	2.922	74.5	25.6
C17	68.99	871.4	25.4	21.9	11	3.2	648	2.514	71.4	28.4
C18	71.13	845.6	23.4	18.8	16	4.5	565	2.922	74.3	25.4
C19	75.01	801	28.3	21.4	24	6.4	591	2.504	71.4	28.5
C20	70.23	861.1	50.9	40.3	38	10.9	2881	3.164	75.8	24
C21	64.36	936.1	41.6	33.8	39	12.2	1404	3.363	77	22.9
C22	73.8	815.3	33.9	24.4	21	5.7	830	3.414	77.3	22.6
C23	69.65	869.6	51	39	36	10.5	2256	2.556	71.8	28.1
C24	70.02	859.9	21.6	16.1	10	2.9	411	2.894	74.2	25.7
C25	70.16	856.2	16	11.1	1	0.3	187	2.884	74.2	25.7
C26	66.47	906.1	44.2	37.1	27	8.2	1469	2.574	71.9	27.9
C27	70.99	850.5	36.9	25.4	17	4.9	1386	1.943	65.9	33.9
C28	71.8	841.1	43.8	35.9	43	12.1	2542	3.114	75.6	24.3
C29	70.39	860.2	58.1	46.9	29	8	1242	2.985	74.8	25.1
C30	66.72	903.4	36.3	27.8	19	5.7	1390	3.43	77.3	22.5

DEEP BREATHING TEST E/I RATIO, VALSALVARATIO AND ISOMETRIC HAND GRIP TEST IN STUDY GROUP

S.No	MEAN HR bpm	MEAN RR ms	SDNN ms	HF nu	E/I RATIO	VALSALVA RATIO	SBP DIFFERENCE mmHg	DBP DIFFERENCE mmHg
O1	70.12	859.9	58.3	30.8	1.118	1.179	8	10
O2	81.25	740.1	28.3	39.4	1.064	1.084	12	12
O3	83.79	717.6	33.3	26.5	1.069	1.417	10	14
O4	79.97	753	40.6	27.9	1.15	1.386	6	8
O5	72.89	829	64.8	28.6	1.176	1.531	14	16
O6	70.69	853.7	48.2	31.3	1.088	1.048	12	8
O7	81.44	740.6	50.7	18.9	1.129	1.153	14	12
O8	63.25	969.3	132.1	22.9	1.18	1.176	10	10
O9	73.62	818.9	47.5	28.9	1.111	1.537	8	12
O10	62.16	969	53.7	27.6	1.088	1.93	10	12
O11	67.76	892.6	73.8	31.5	1.18	1.361	10	14
O12	63.82	952.6	100.8	17.3	1.295	1.672	10	10
O13	62.75	969.2	108.2	26.4	1.202	1.121	14	14
O14	72.83	844.3	122.4	36.9	1.354	1.174	16	12
O15	71.43	851.5	93.8	33.9	1.282	1.61	8	10

S.No	MEAN HR bpm	MEAN RR ms	SDNN ms	HF nu	E/I RATIO	VALSALVA RATIO	SBP DIFFERENCE mmHg	DBP DIFFERENCE mmHg
O16	69.22	902	154.1	32.4	1.469	1.294	8	8
O17	85.66	703.9	33.9	25.1	1.131	1.648	10	14
O18	76.16	793.1	60.9	41.4	1.276	1.088	16	12
O19	77.32	783	69.6	25.7	1.202	1.4	8	4
O20	77.37	786.1	85.8	31	1.276	1.088	8	8
O21	79.62	762.5	54.9	31.1	1.108	1.287	6	6
O22	91.84	654.2	21.7	48.5	1.158	1.359	10	12
O23	64.06	962	144.4	26.4	1.487	1.436	8	14
O24	62.84	967	105.3	28.9	1.264	1.385	10	8
O25	85.53	702.8	25.3	19	1.073	1.044	8	8
O26	94.04	643.2	46.7	42.3	1.033	1.104	12	8
O27	79.73	758.7	64.3	34.3	1.193	1.06	8	12
O28	77.03	782	38.3	37.2	1.13	1.276	14	12
O29	85.68	703.5	39	24	1.121	1.434	8	12
O30	73.96	820.2	86	43.7	1.251	1.216	10	12

DEEP BREATHING TEST E/I RATIO, VALSALVARATIO AND ISOMETRIC HAND GRIP TEST IN CONTROL GROUP

SNO	MEAN HR bpm	MEAN RR ms	SDNN ms	HF nu	E/I RATIO	VALSALVA RATIO	SBP DIFFERENCE mmHg	DBP DIFFERENCE mmHg
C1	80.68	760.6	94.9	31.7	1.226	1.208	10	10
C2	87.23	707.5	88.2	39.3	1.243	1.949	16	14
C3	70.15	861.4	61.8	33.4	1.154	1.288	8	10
C4	74.4	816.5	84.9	33.4	1.251	1.317	8	8
C5	81.91	755.2	121.6	80.5	1.524	1.415	16	10
C6	70.46	892.2	185.1	35.5	1.126	1.575	10	14
C7	71.34	863.8	133.2	37.8	1.404	1.4983	14	18
C8	83.17	739.2	115.4	39.5	1.361	2.352	8	14
C9	72.44	833.1	56.1	30.7	1.118	1.282	10	12
C10	73.7	832.4	123	28.5	1.334	1.26	16	16
C11	82	748.7	108.2	35.9	1.366	1.754	10	16
C12	83.89	729.2	89.6	33.3	1.29	1.375	10	8
C13	76.93	796.9	100.9	26.3	1.27	1.385	10	14
C14	70.91	862.9	118.5	37.6	1.358	1.507	8	12
C15	89.53	673.4	43.4	57	1.27	1.476	10	8
C16	67.24	900	71.3	27.7	1.167	1.874	16	16

SNO	MEAN HR bpm	MEAN RR ms	SDNN ms	HF nu	E/I RATIO	VALSALVA RATIO	SBP DIFFERENCE mmHg	DBP DIFFERENCE mmHg
C17	75.32	806	74.7	23.7	1.192	1.294	10	10
C18	83.11	729.3	66.6	36.8	1.219	1.144	8	12
C19	77.91	780.1	65.8	35.2	1.18	1.202	18	14
C20	76.04	814.4	106.9	38.2	1.326	1.451	20	14
C21	57.49	1051.6	75.2	23.1	1.145	1.409	20	16
C22	70.36	867.9	107	35.9	1.285	1.144	16	16
C23	80.08	760.8	88.7	37.2	1.304	1.521	12	10
C24	67.23	916.1	142.6	31.3	1.409	1.31	18	14
C25	80.33	764.6	114.4	35.5	1.4	1.716	8	14
C26	61.8	988.8	122.2	23.9	1.318	1.381	10	8
C27	74.86	809.5	61.1	40.8	1.141	1.4752	8	10
C28	80.21	763.2	95.7	34	1.433	1.878	12	10
C29	68.55	896.8	122.9	39.7	1.305	1.4841	10	14
C30	76.95	810.6	114.4	31.6	1.373	1.22	18	14